EFFECTS OF CALCINATION AND PARTICLE SIZE ON THE SINTERING OF NATURAL HYDROXYAPATITE

by

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ABSTRACT

EFFECTS OF CALCINATION AND PARTICLE SIZE ON THE SINTERING OF NATURAL HYDROXYAPATITE

The aim of this thesis was to investigate the best suitable method for the production of hydroxyapatite from fresh bone and to determine the effects of reducing the particle size of the hydroxyapatite powder on the microstructural properties and sintering characteristics of the final structures. For this purpose hydroxyapatite powder was obtained from fresh calf bone by deproteinization with NaOH and calcination with different processing parameters. Following this, the powders were ground by ball milling to decrease the particle size. The so produced fine hydroxyapatite powders were investigated by FTIR, X-Ray, EDAX and ESEM images and compared with each other, with ungrounded natural hydroxyapatite and with a inorganically produced, commercial hydroxyapatite. The produced hydroxyapatite powders were sintered at different times and temperatures and microstructural properties and the sintering characteristics of the final products were determined and compared with each other by EDAX analyses and ESEM images. Finally, effects of boron oxide as an additive on the sintering of hydroxyapatite were investigated.

Keywords: Hydroxyapatite, ceramics, grinding, calcination, sintering, boron oxide.

ÖZET

KALSİNASYON VE PARÇACIK BOYUTUNUN DOĞAL HİDROKSİAPATİTİN SİNTERLENMESİ ÜZERİNE ETKİLERİ

Bu tezin amacı; taze kemikten hidroksiapatit üretimine yönelik en iyi yöntemin araştırılması ve hidroksiapatit tozunun parçacık boyutunun azaltılmasının son ürünün mikroyapısal özellikleri ve sinterleme karakteristiklerine ektilerini incelemektir. Bu amaçla; taze dana kemiğinden farklı NaOH deprotenizasyonu ve kalsinasyon değişkenleri kullanılarak hidroksiapatit tozu elde edilmiştir. Bunun ardından, parçacık boyutunu küçültmek amacıyla tozlar bilyalı değirmende öğütülmüştür. Bu şekilde üretilen küçük boyutlu hidroksiapatit tozları FTIR, X-Işını, EDAX ve ESEM görüntüleri aracılığıyla birbirleriyle, öğütülmemiş doğal hidroksiapatitle ve inorganik olarak sentezlenmiş, ticari bir hidroksiapatitle karşılaştırılmıştır. Üretilen tozlar farklı zaman ve sıcaklıklarda sinterlenmiş ve son ürünlerin mikroyapısal özellikleri ve sinterleme karakteristikleri EDAX analizi ve ESEM resimleri aracılığıyla belirlenmiştir ve birbirleriyle karşılaştırılmıştır. Son olarak, bir sinterleme katkısı olarak bor oksitin hidroksiapatitin sinterlenmesi üzerine etkileri incelenmiştir.

Anahtar kelimeler: Hidroksiapatit, seramik, öğütme, kalsinasyon, sinterleme, bor oksit.

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LIST OF SYMBOLS / ABBREVIATIONS

ω	Angular velocity
$\bar{a}$	Average particle size
n	Weibull factor
R	Radius
T_g	Glass transition temperature
rpm	Revolutions per minute
wt.	Weight
HA	Hydroxyapatite (or hydroxylapatite)
HAp	Hydroxyapatite (or hydroxylapatite)
PE	Polyethylene
PLA	Polylacticacid
PMMA	Polymethylmethacrylate
PU	Polyurethane
SS	Stainless steel
TCP	Tricalcium phosphate
EDAX	Energy dispersive analysis of X-rays
ESEM	Environmental scanning electron microscope
FTIR	Fourier transform infrared
FT-IR	Fourier transform infrared
TEM	Transmission electron microscope
XRD	X-Ray diffraction

1. INTRODUCTION

A biomaterial is a synthetic material used to replace part of a living system or to function in intimate contact with living tissue. More formally, a biomaterial is a systemically and pharmacologically inert substance designed for implantation within or incorporation with living systems. Another, more general definition found in literature is "a biomaterial is a nonviable material used in a medical device, intended to interact with biological systems [1, 2].

Alternative to the biomaterials are autografts (healthy tissue obtained from the patient), allografts (healthy tissue obtained from another member of the same species), and xenografts (healthy tissue obtained from a member of another species) [3]. However, except autografts, they posses the danger of disease transfer and increased possibility of rejection by the host body [4]. On the other hand, autografts do not have the danger of disease transfer since it is healthy tissue of the patient himself and the possibility of rejection is definitely lower but using autografts requires a primary operation in order to obtain the autograft and a following one for the implantation. In many cases this can be hard for the patient. In all the types of grafts preservation of the healthy tissue and manufacturing of it into the desired dimensions for the implantation can be a tedious problem and there is no tolerance for any possible mistake prior to operation, especially for atuografts and allografts.

Therefore, design and production of suitable biomaterials are of great importance in decreasing the necessary number of operations and also the danger of disease transfers. Biomaterials can much easily be shaped into the necessary dimensions of the implant and in case of any mistake prior to the operation another implant can be used.

Members from all the four groups of materials, namely polymers, metals, ceramics and composites, can be used as biomaterials as far as they satisfy certain conditions. A biomaterial of question must not cause an attack of the body's immune system and

should have an acceptable or better no toxicity, leading to and inflammation or causing cancer. These can be summarized under the term "biocompatibility".

Table 1.1. Materials for use in the body [1]

Materials	Advantages	Disadvantages	Examples
Polymers : Nylon Silicones Teflon Dacron	Resilient Easy to fabricate	Not strong Deform with time May degrade	Sutures, blood vessels, hip socket, ear, nose, other soft tissues
Metals : Titanium Stainless steels Co-Cr alloys Gold	Strong, though Ductile	May corrode Dense	Joint replacement, bone plates and screws, dental root implants
Ceramics : Aluminum oxide Carbon Hydroxyapatite	Very biocompatible, inert Strong in compression	Brittle Difficult to make Not resilient	Dental, hip socket
Composites : Carbon-carbon	Strong, tailor-made	Difficult to make	Joint implants, heart valves

Biomaterials are used in the replacement of diseased or damaged part (e.g., artificial hip joint, kidney analysis machine), assisting in healing (e.g., sutures, bone plates and screws), improvement of function (e.g., cardiac pacemaker, contact lens), correction of functional abnormality (e.g., Harrington spinal rod), correction of cosmetic problems e.g., (augmentation mammoplasty, chin augmentation), aiding the diagnosis (e.g., probes and catheters) and aiding to treatment (e.g., catheters, drains).

Table 1.2. Applications of synthetic and modified natural materials in medicine [1, 2]

Application	Examples	Type of Materials
Skeletal and muscular system	Joint replacements	Ti, Ti-Al-V alloy, stainless steel, PE
	Bone plate for fracture fixation	Stainless steel, Co-Cr alloy
	Bone cement	PMMA
	Bony defect repair	Hydroxyapatite
	Artificial tendon and ligament	Teflon, dacron
	Dental implant for tooth fixation	Ti, alumina, calcium phosphate
Cardiovascular system	Blood vessel prosthesis	Dacron, Teflon, PU
	Heart valve	Reprocessed tissue, SS, carbon
	Catheter	Silicone rubber, Teflon, PU
Organs (heart, lung, kidney, bladder)	Artificial heart	PU
	Skin repair template	Silicone-collagen composite
	Artificial kidney	Cellulose, polyacrylonitrile
	Heart-lung machine	Silicone rubber
Senses (eye, ear)	Cochlear	Platinum electrodes,
	Intraocular lens	PMMA, silicone rubber, hydrogel
	Contact lens	Silicone-acrylate, hydrogel
	Corneal bandage	Collagen, hydrogel
PE	Polyethylene	
PMMA	Polymethylmethacrylate	
PU	Polyurethane	
SS	Stainless Steel	

Biocompatibility involves the acceptance of an artificial implant by the surrounding tissues and by the body as a whole. More formally, it is the ability of a material to perform with an appropriate host response in a specific application [1, 2].

In addition to its biocompatibility characteristics an implant material should also posses other necessary mechanical, electrical and optical properties which are important from the engineering point of view. These include density, porosity, permeability, strength, stiffness, and fatigue properties, and manufacturability.

2. BIOCERAMICS

2.1. Bioceramics

Ceramics are refractory and polycrystalline materials which are usually inorganic. Ceramics include ionic salts, silicates, metallic oxides, carbides, hydrides, sulfides, selenides, and apatites.

Ceramics have been satisfactory candidates as implant materials owing to their desirable characteristics such as inertness to body fluids, high compressive strength, and good esthetic appearance. As a result, they have been widely used to repair or replace skeletal hard tissues such as bone and tooth. They can make up the entire implant, or they can be applied in the form of a coating onto a metallic core. Coatings can be dense or porous, depending on the chemical composition of the parent material and the coating method that is employed [5].

Table 2.1. Present uses of bioceramics [2]

Application	Type of bioceramic
Orthopedic lead-bearing applications	Al_2O_3
Coatings for chemical bonding (orthopedic, dental, and maxilofacial prosthetics)	Hydroxyapatite Bioactive glasses Bioactive glass-ceramics
Dental implants	Al_2O_3 Hydroxyapatite Bioactive glasses
Alveolar ridge augmentations	Al_2O_3 Hydroxyapatite Hydroxyapatite-autogenous bone composite Hydroxyapatite-PLA composite Bioactive glasses

Table 2.1. Present uses of bioceramics [2] (Cont.)

Application	Type of bioceramic
Otolaryngological	Al_2O_3 Hydroxyapatite Bioactive glasses Bioactive glass-ceramics
Artificial tendon and ligament	PLA-carbon fiber composite
Coating for tissue ingrowth (cardiovascular, orthopedic, dental and maxilofacial prosthetics)	Al_2O_3
Temporary bone space fillers	Tricalcium phosphate Calcium and phosphate salts
Periodontal pocket obliteration	Hydroxyapatite Hydroxyapatite-PLA composite Trisodium phosphate Calcium and phosphate salts Bioactive glasses
Maxiofacial reconstruction	Al_2O hydroxyapatite Hydroxyapatite-PLA composite Bioactive glasses
Percutaneous access devices	Bioactive glasses Bioactive composites
Orthopedic fixation devices	PLA-carbon fibers PLA-calcium/phosphorus-base glass fibers

There are four types of bioceramics, namely, inert, allowing porous ingrowth, bioactive and resorbable.

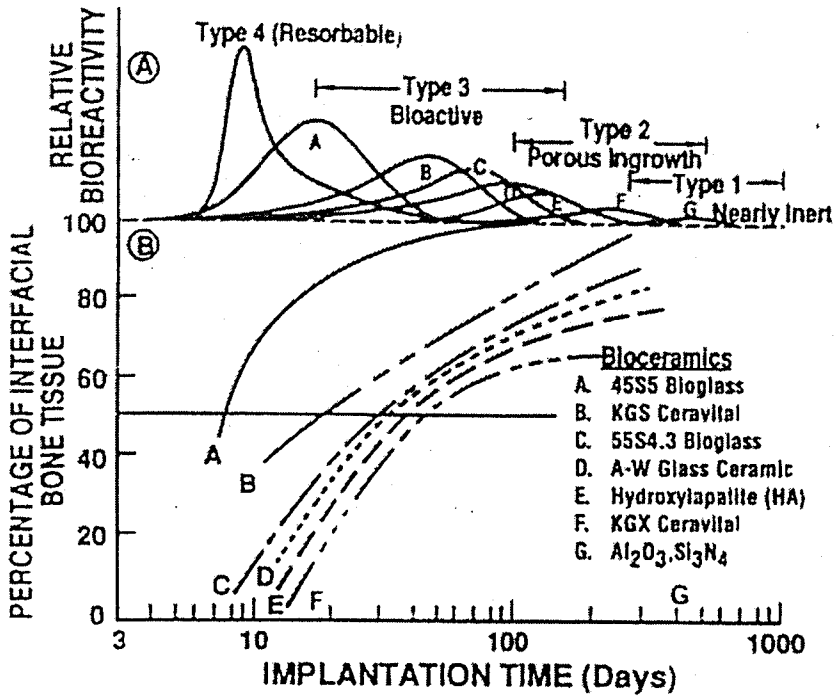

Figure 2.1. Bioactivity spectra for various bioceramic implants: (a) relative rate of bioreactivity, (b) time dependence of formation of bone bonding at an implant interface [2]

Accordingly, between four different conditions of implant fixation can be differentiated. These are:

Morphological fixation: Dense, nonporous, nearly inert ceramics attach by bone growth into surface irregularities by cementing the device into the tissues or by press-fitting into a defect, e.g. Al_2O_3 (single crystal and polycrystalline).

Biological fixation: For porous inert implants, bone ingrowth occurs that mechanically attaches the bone to the material, e.g. Al_2O_3 (polycrystalline), hydroxyapatite-coated porous metals.

Bioactive fixation: Dense, nonporous surface-reactive ceramics, glasses, and glass-ceramics attach directly by chemical bonding with the bone, e.g. bioactive glasses, bioactive glass-ceramics, hydroxyapatite.

Resorbable implant: Dense, nonporous (or porous) resorbable ceramics are designed to be slowly replaced by bone, e.g. calcium sulfate (plaster of paris), tricalcium phosphate, calcium-phosphate salts.

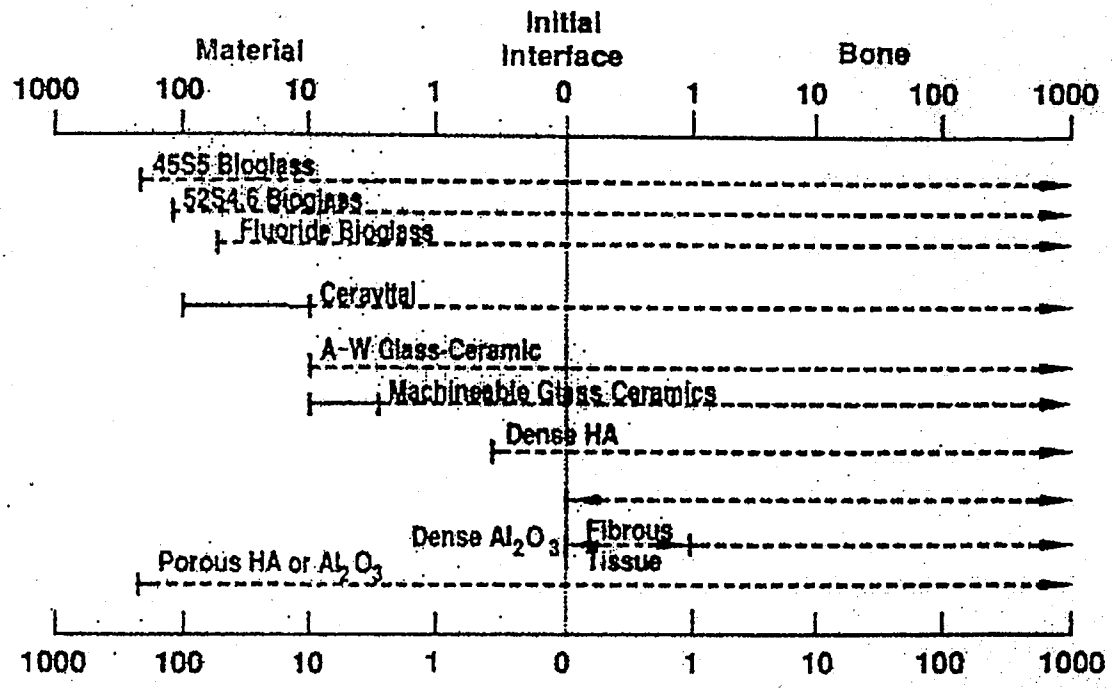

Figure 2.2. Comparison of interfacial thickness (μm) of reaction layer of bioactive implants of fibrous tissue of inactive bioceramics in bone [2]

2.2. Porous Ceramics

Ceramics can be produced with a range of porosities depending on the method of processing [6]. In no-load-bearing applications porous ceramics can act as a satisfactory implant material. However, porous materials are weaker than the equivalent bulk form in proportion to the percentage of porosity and with increasing porosity the strength of the material decreases rapidly. Since with increasing porosity much surface area is also exposed, the effects of the environment on decreasing the strength become much more important then for dense, nonporous materials. Therefore, the aging of porous ceramics, with their subsequent decrease in strength, requires bone ingrowth to stabilize the structure of the implant. And clinical results have proven positively that porous ceramics are good materials for no-load-bearing applications.

When the pore size is more than 100 μm, bone can grow within the interconnecting pore channels near the surface and maintain its vascularity and long-term viability. In this case, the implant serves as a structural bridge or scaffold for bone formation [2].

The porosity can be classified according to pore diameter as macroporosity (> 10 μm) and microporosity (< 10 μm) and it has been suggested that these structural modifications influence the biocompatibility of hydroxyapatite. The larger the macropores, the more tissue ingrowth is possible if the pore diameter is greater than 150 μm, the ideal value suggested being between 300 and 400 μm [6]. Joschek *et al.* [4] have found that the average pore size to be 317 ± 9 μm and 1.33 ± 0.18 μm for the macro- and micropores, respectively.

Micropores help to establish connections between the macropores, which allows interstitial fluid circulation through them. This event would facilitate blood vessel and tissue ingrowth in the implant. Also, interconnected micropores are important because their presence allows the implant to be machinable. However, recent research has shown that an increase in micropore percentage negatively influences the biocompatibility [6].

3. HYDROXYAPATITE

3.1. Calcium Phosphate

The development of calcium phosphate ceramics and other related biomaterials for bone graft involved a better control of the process of biomaterials resorption and bone substitution [7]. Therefore, calcium phosphate based bioceramics have been used in medical and dental applications for over two decades.

Calcium phosphate ceramics are widely preferred in implants for their established history of safety and efficacy as biocompatible implantable materials [3]. Their applications include dental implants, periodontal treatment, alveolar ridge augmentation, orthopedics, maxillofacial surgery, and otolaryngology.

Depending on the requirements whether a resorbable or a bioactive material is required different phases of calcium phosphates can be used.

Calcium phosphate can be crystallized into salts, hydroxyapatite and β-tricalcium phosphate depending on the Ca/P ratio, presence of water, impurities, and temperature [1].

The stable phases of calcium phosphate ceramics depend on the ambient temperature and the presence of water during processing or in the environment. In a wet environment and at lower temperature (<900 °C) it is more likely that hydroxyapatite will form whereas in a dry atmosphere and at higher temperature β-tricalcium phosphate will be formed [1, 2].

Both forms are very tissue compatible and are used for bone substitute in a granular form or a solid block. On the other hand, hydroxyapatite is more closely related to the mineral phase of bone and teeth.

At body temperature and in body fluid only two calcium phosphates are stable. At pH<4.2 the stable phase is $CaHPO_4 \bullet 2H_2O$ (dicalcium phosphate) whereas at pH≥4.2 the stable phase is $Ca_{10}(PO_4)_6(OH)_2$ (hydroxyapatite) [2].

At higher temperatures other phases such as $Ca_3(PO_4)_2$ (β-tricalcium phosphate) and $Ca_4P_2O_9$ (tetracalciumphosphate) are present [2].

The unhydrated high-temperature calcium phosphate phases interact with water or body fluids at 37 °C to form hydroxyapatite. Hydroxyapatite forms on exposed surfaces of tricalcium phosphate by the below reaction:

$$4\ Ca_3(PO_4)_2\ (solid) + 2\ H_2O \rightarrow Ca_{10}(PO_4)_6(OH)_2\ (surface) + 2\ Ca^{2+} + 2\ HPO_4^{2-}$$

Thus, the solubility of a tricalcium phosphate surface approaches the solubility of hydroxyapatite and decreases the pH of the solution, which further increases the solubility of tricalcium phosphate and enhances resorption [2].

The presence of micropores in the sintered material can increase the solubility of these phases [2].

Sintering of calcium phosphate ceramics usually occur in the range of 1000-1500 °C following compaction of the powder into a desired shape.

The phases formed at high temperature depend not only on temperature but also on the partial pressure of water in the sintering atmosphere since with water present hydroxyapatite can be formed and is a stable phase up to 1360 °C [2].

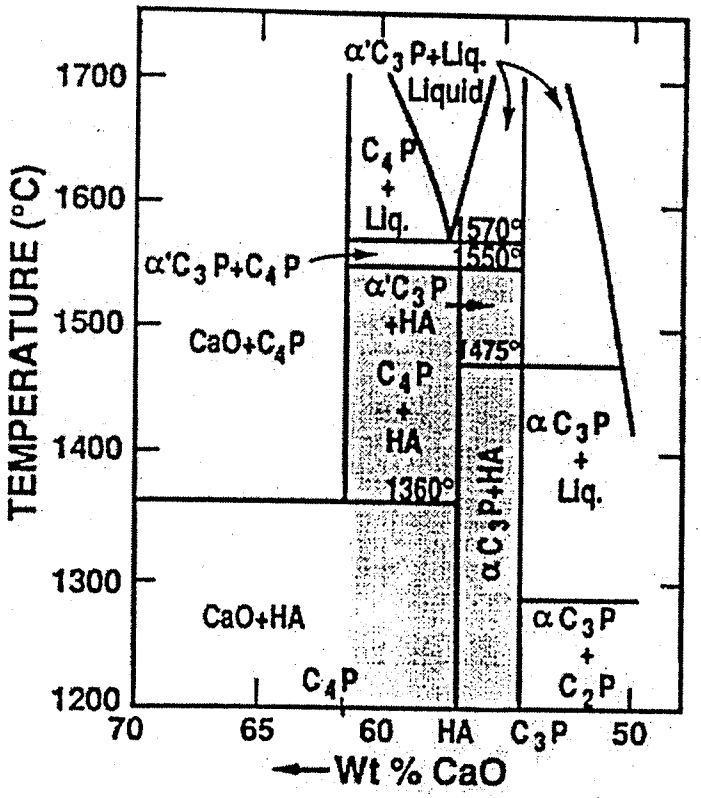

Figure 3.1. Phase equilibrium diagram of calcium phosphates in a water atmosphere. Shaded area is processing range to yield hydroxyapatite-containing implants [2]

The temperature range of stability of hydroxyapatite increases with the partial pressure of water. Because of kinetics barriers that affect the rates of formation of the stable calcium phosphate phases, it is often difficult to predict the volume fraction of high-temperature phases that are formed during sintering and their relative stability when cooled to room temperature.

Table 3.1. Physical properties of calcium phosphate [1]

Property	Value
Elastic modulus (GPa)	40-117
Compressive strength (MPa)	294
Bending strength (MPa)	147
Hardness (Vickers, GPa)	3.43
Poisson's ratio	0.27
Density (theoretical, g/cm^3)	3.16

The mechanical behavior of calcium phosphate ceramics strongly influences their application as implants. Tensile and compressive strength and fatigue resistance depend on the total volume of porosity. Porosity can be in the form of micropores (<1 μm diameter, due to incomplete sintering) or macropores (>100 μm diameter, created to permit bone growth). The dependence of compressive and tensile strengths on the total pore volume is given by the following equations [2]:

$$\sigma_c = 700e^{-5V_p}$$

where; σ_c is compressive strength in MPa and V_p is total pore volume in the range of 0-0.5, and

$$\sigma_t = 220e^{-20V_m}$$

where; σ_t is tensile strength in MPa and V_m is volume fraction of microporosity.

The small Weibull factor (n=12) of hydroxyapatite implants in physiological solutions indicates low reliability under tensile loads. Therefore, calcium phosphate ceramics should be used as powders, coatings, small and unloaded implants, with reinforcing metal posts and low loaded porous implants where bone growth acts as a reinforcing phase [2].

3.2. Hydroxyapatite

Hydroxyapatite shows excellent biocompatibility because the mineral part of bone and teeth is a crystalline form of calcium phosphate similar to hydroxyapatite. Therefore, hydroxyapatite has an important role in producing ceramic implants as it appears to form a direct chemical bond with hard tissues. Hydroxyapatite can appear in either crystalline or amorphous form and its crystalline structure can be altered by subsequent heat treatments [5].

The ideal Ca/P ratio of hydroxyapatite is 10:6 and the calculated density is 3.219 g/cm^3. The apatites, having the form of $A_{10}(BO_4)_6X_2$, crystallize into hexagonal rhombic prisms and have unit cell dimensions of a=9.432 $\mathring{A}$ and c=6.881 $\mathring{A}$.

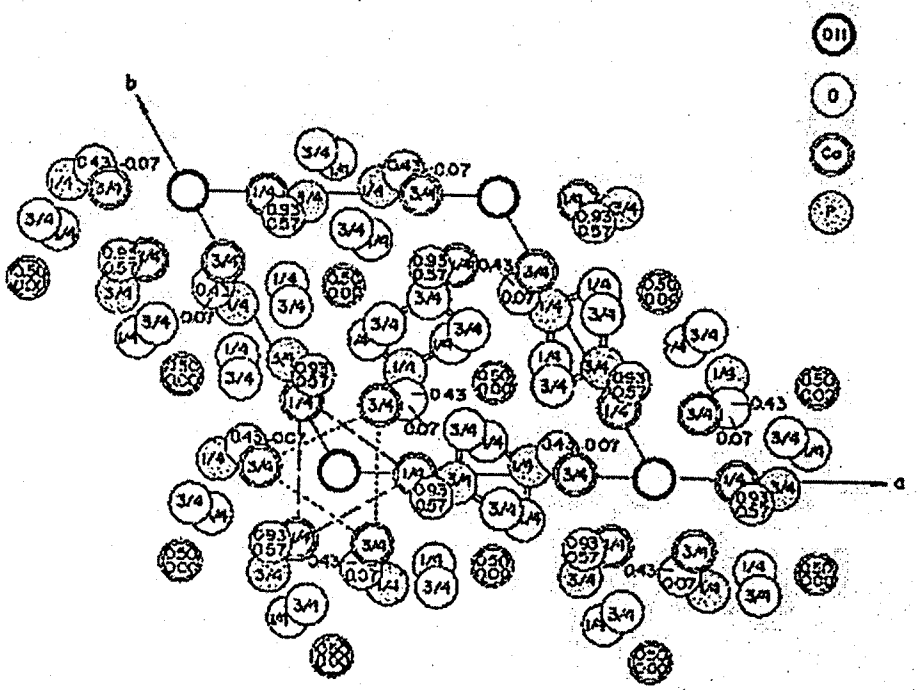

Figure 3.2. Hydroxyapatite structure projected down the c axis onto the basal plane [1]

As noted in the above figure, the hydroxyl ions lie on the corners of the projected basal plane and they occur at equidistant intervals one-half of the cells along columns perpendicular to the basal plane and parallel to the c axis. Six of ten calcium ions in the unit cell are associated with the hydroxyls in these columns, resulting in strong interactions among them.

The substitution of OH^- ions with F^- ions will give greater chemical stability due to the closer coordination of F (symmetric shape) as compared to the hydroxyl (nonsymmetrical, two atoms) by the nearest calcium. This explains the better caries resistance of teeth following fluoridation [1].

The variation of properties of the final product is a direct result of the variation in the structure of polycrystalline calcium phosphates, which is in turn the result of

differences in manufacturing processes. Final firing conditions greatly influence the hydroxyapatite and β-tricalcium phosphate composition of the final product, however, both types of structure exist in the final product.

There are different techniques to make precipitates of hydroxyapatite from an aqueous solution of $Ca(NO_3)_2$ and NaH_2PO_4. In the mostly used technique, precipitates are filtered and dried to form a fine particle powder. The powder is calcined for about 3 hours at 900 °C to promote crystallization, pressed into a final form and sintered at about 1050-1200 °C for 3 hours. Above 1250 °C the hydroxyapatite shows a second phase precipitation along the grain boundaries [1].

The formation of the bond between hydroxyapatite and the bone seems to result from the physicochemical interaction between the ceramics and the interfacial fluid, in the sense of dissolution/resorption, and epitaxial growth [8]. Regarding the bonding process of hydroxyapatite implants, a cellular bone matrix from differentiated osteoblasts appears at the surface, producing a narrow amorphous electron-dense band only 3-5 μm wide. Between this area and the cells, collagen bundles are seen. Bone mineral crystals have been identified in this amorphous area. As the site matures, the bonding zone shrinks to a depth of only 0.05-0.2 μm. The result is normal bone attached through a thin epitaxial bonding layer to the bulk implant. TEM image analysis of dense hydroxyapatite bone interfaces show an almost perfect epitaxial alignment of some of the growing bone crystallites with the apatite crystals in the implant. A consequence of this ultra thin bonding zone is a very high gradient in elastic modulus at the bonding interface between hydroxyapatite and bone [1].

Biodegradation or resorption of calcium phosphate ceramics in general is caused by three different factors. First of these factors is physicochemical dissolution, which depends on the solubility product of the material and local pH of its environment. New surface phases may be formed, such as amorphous calcium phosphate, dicalcium phosphate, dicalcium phosphate dehydrate, octacalcium phosphate, and anionic-substituted hydroxyapatite due to this. Next factor is physical disintegration into small particles as a result of preferential chemical attack of grain boundaries. And the last one

is a biological factor, such as phagocytosis, which causes a decrease in local pH concentration [1].

All calcium phosphate ceramics biodegrade to varying degrees in the following order:

α-tricalcium phosphate > β-tricalcium phosphate >> hydroxyapatite

increasing rate →

meaning that, the degradation of β-tricalcium phosphate into hydroxyapatite is more intense than the degradation of α-tricalcium phosphate into β-tricalcium phosphate.

The rate of biodegradation increases as the surface area increases (powders>porous solid>dense solid), crystallinity, crystal perfection and crystal and grain sizes decrease and if there are ionic substitutions of CO_3^{2-}, Mg^{2+}, and Sr^{2+} in hydroxyapatite [9]. Oppositely to these, F^- substitution in hydroxyapatite, Mg^{2+} substitution in β-tricalcium phosphate, and lower β-tricalcium phosphate/hydroxyapatite ratios in biphasic calcium phosphates decrease the rate of biodegradation [1].

3.3. Production of Hydroxyapatite

Mainly, there are three ways of producing hydroxyapatite. The first one is obtaining hydroxyapatite from natural sources of hydroxyapatite, like bone and tooth. Next way is to react calciumphosphate containing natural minerals, like egg shell or coral, with several chemicals. And the final way is synthesizing hydroxyapatite from different chemicals without use of any natural sources.

Tas states that bone mineral has commonly been referred to the perfectly stoichiometric compound hydroxyapatite , but it actually is a defective and complex substance doped with several cations and that stoichiometric synthetic hydroxyapatite do not participate in bone remodeling [10]. Therefore, among the above stated methods

the first one, namely obtaining hydroxyapatite from natural sources is the most meaningful one for the biomedical applications.

3.3.1. Obtaining Hydroxyapatite from Natural Sources

Obtaining hydroxyapatite from natural sources such as bone and tooth is a suitable method in the production of hydroxyapatite for use in biomedical applications like implants, bone cements and surface coating. It is an inexpensive as well as a less complicated method compared to the synthesizing hydroxyapatite from various chemicals. Especially the methods where high temperatures are applied offer high security against the possibility of disease transfer because it is well known that no organic substance can survive such high temperatures. Additionally, the hydroxyapatite obtained from organic sources is the same material found in living bone and tooth whereas the synthesized hydroxyapatites can only resemble their natural counterparts.

Murugan *et al.* [11] showed the possibility of preparing protein-free inorganic minerals of xenogenic bone by simple calcination of bone at various temperatures ranging from 500 to 900 °C. The heat deproteinated bone corresponded to hydroxyapatite and phase purity of the so obtained mineral has been confirmed by XRD and FTIR analyses. They have concluded that the organic phase of the bone has been eliminated at 500 °C.

Mittelmeier *et al.* [12] applied pyrolization at elevated temperatures from 400 to 1500 °C after dealbumination in H_2O_2 to produce hydroxyapatite from raw bone.

On the other hand, Bauer *et al.* [13] completely eliminated any step containing chemical treatment and were able to produce hydroxyapatite from raw bone by controlled calcination at temperatures from 550 to 800 °C.

Johnson *et al.* [14] and Anderson *et al.* [15] showed that chemical treatment of bone with NaOH, NaOCl and H_2O_2 can also be an alternative in the preparation of bone substitutes.

Joshi *et al.* [16] examined the suitability of tooth derived hydroxyapatite for plasma spraying applications. They calcined human teeth at 650 °C to obtain hydroxyapatite and they successfully used it in plasma spraying.

The previous studies conducted in the Materials and Manufacturing Laboratory of Boğaziçi University includes the production of hydroxyapatite from human teeth and from calf femur [17-19]. Gokbayrak and Goren investigated the production of hydroxyapatite from calf femur by chemical deproteinizaiton method [18, 19]. They all employed chemical deproteinization techniques followed by the calcination of the samples in order to obtain hydroxyapatite.

3.3.2. Synthesizing Hydroxyapatite from Calcium Containing Natural Sources

This way is an intermediate path between obtaining hydroxyapatite from natural sources and synthesizing it from various chemicals. It is an inexpensive method as the above one. However, obtaining pure hydroxyapatite is not guaranteed through these processes, however, research still continues.

Sivakumar *et al.* [20] reacted calcium containing minerals obtained from the calcination of Indian coral with diammonium phosphate succesfully to produce calcium phosphates. However, the resulting material was not purely hydroxyapatite.

3.3.3. Synthesizing Hydroxyapatite from Various Chemicals

A great variety of methods for the synthesis of hydroxyapatite is known which can be subdivided into wet, dry and hydrothermal methods.

Dry methods are based on the fact that solid ingredients when heated to an optimum temperature can lead to the formation of a desired lattice through solid state diffusion of the constituent ions. For this purpose two different constituents containing calcium and phosphate ions are reacted at high temperatures under the presence of moisture. These methods are used for the production of hydroxyapatite of accurate

stoichiometric composition of Ca/P ratio equal to 1.67. However, since they need to be carried out at relatively high temperatures between 1000 and 1400 °C they are expensive [18, 19, 21].

The wet method is based on the idea of reacting two chemicals one of which is acting as the calcium source whereas the other one supplies the phosphate ions and letting the resulting hydroxyapatite precipitate from the solution by controlling the pH. Through varying the Ca/P ratio it is also possible to obtain different types of calcium phosphates.

Mostly, $CaCl_2$, $Ca(NO_3)_2$ and $Ca(OH)_2$ are used as the source for calcium and H_3PO_4, $(NH_4)HPO_4$ and KH_2PO_4 for phosphate ions. The acidity is usually controlled by appropriate application of gaseous ammonia, ammonium hydroxide and sodium hydroxide [18, 19, 21].

Wet methods are preferred because of their simplicity to realize without the use of any special equipment and high temperature furnaces. Control of the precipitate formation is the only necessary point to be paid attention to. Through the use of the wet methods it is possible to obtain large quantities of highly pure hydroxyapatite.

As its name implies, hydrothermal methods deal with the application of high temperatures to aqueous solutions to facilitate the precipitation of crystals of dimensions larger than those obtainable through wet methods. To increase the boiling point of the precipitating medium in order to increase the overall temperature of the constituents usually higher pressures than the atmospheric one are applied. As a result, highly crystalline and pure hydroxyapatite can be produced through the use of hydrothermal methods.

4. CALCINATION

Calcining refers to a high-temperature treatment of a powder to modify the characteristics of the powder. Calcining, in general, leads to coarsening, decomposition, reaction and dehydration.

Coarsening involves crystallite growth or fusing or bonding small particles together to produce larger particles whereas decomposition involves converting compositions such as carbonates and nitrates to oxides. Gases are evolved during the decomposition reactions that could build up enough pressure to crack a powder compact. Therefore, the decomposition is sometimes achieved by calcining the powder prior to compaction. Prereacting powders is sometimes conducted for the same reason. Dehydration is important in preparation of hydraulic cements and plaster. Addition of water to powder afterwards results in rehydration [22].

Time and temperature are important variables in calcination but temperature has a greater role in the process. Maximum size of agglomerates or segregated materials in the batch is also of importance. Further, particle size distribution of the material, the composition and flow of gases and the ambient atmospheric variables are determining factors in the calcination process [23].

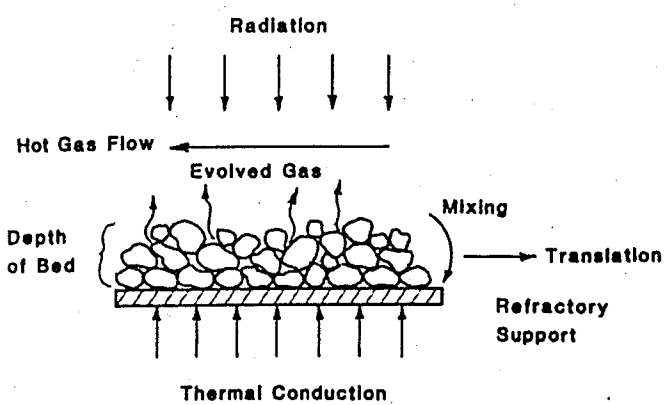

Figure 4.1. Thermal transport, gas flow, and particle movement during rotary calcination [23]

4.1. Calcination of Hydroxyapatite

Juang *et al.* [24] found that sintering begins at higher temperatures for calcined hydroxyapatite and that for samples calcined at 800 °C or over the shrinkage rate decreases. This is indicative for the necessity of higher temperatures to reach the final stage of sintering. Calcination at 700 °C and below is found not to affect the sintering behavior of hydroxyapatite significantly. Further, calcination changes the particle size distribution of the powder from multi-modal to uni-modal because of coalescence of finer particles during calcination, but no phase transformation occurs. Finer particles of the uncalcined powder provides more surface as driving force of sintering; however, van der Waals force then becomes more significant, which retards the packing of the powder. Thus, calcination is found to increase the efficiency of powder packing though driving force is sacrificed. Powder calcined at 900 °C and sintered at 1250 °C results in the best mechanical properties.

Similarly, Patel *et al.* [25] states that non-calcined hydroxyapatite starts to sinter at relatively low temperatures like 800 ° whereas on the other hand, a relatively high calcination temperature close to 1000 °C results in a decrease in the properties of the calcined hydroxyapatite.

Fanovich *et al.* [26] has stated that a relatively high temperature treatment results in the decrease of the surface area of the particles which further would result in reduced densification of the powder during sintering.

Raynaud *et al.* [27] found that calcination changed the small agglomerated needle-like crystals into more rounded particles and led to the formation of necks between these particles.

5. PARTICLE SIZE REDUCTION

Control of particle size and particle size distribution is required to achieve the optimum properties for an intended application. Each application has its own specific requirements. For example, a ceramic which is intended to be used as a high-strength material should have very fine particles (usually less than 1 μm) [22]. To obtain a desired average particle size and a desired particle size distribution regarding the requirements of the application in consideration, first of all, techniques like screening, classifying or elutriation are used.

However, usually the above stated techniques are not sufficient to obtain the desired average particle size and particle size distribution. In such cases a particle size reduction (communition) step is necessary. The communition processes like crushing and milling are widely used in ceramic processing in order to reduce the average and maximum particle size of a material, to modify the particle size distribution and to disperse agglomerates and aggregates [23].

5.1. Communition Equipment

There are many different communition techniques. The most important point they have in common is that they all use mechanical forces to reduce the size of the existing particles.

Crushers like jaw and cone crushers are used to produce compression and shear stresses to reduce the size of coarse feed to an average size down to 5 mm. Crushing rolls can reduce the size of less coarse feed to below 1 mm. Rotating hammers pulverize particles in a hammer mill, reducing them down to 0.1 mm in size [23].

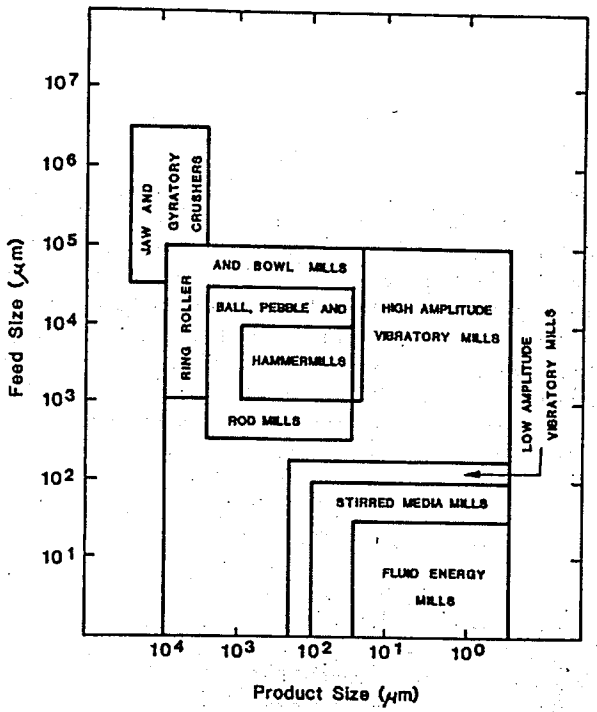

Figure 5.1. Nominal feed and product mean size capabilities of industrial equipment [23]

After the primary size reduction ball, attrition, vibratory and fluid energy mills can be used for further reducing of the particle size.

A ball mill is simply a hollow cylinder in which the material to be ground and the grinding media are placed. The ball mill can be a plastic or ceramic jar or a steel shell. The grinding media are hard, wear-resistant material usually in the shape of rods, short cylinders or, most commonly, balls. The ball mill is rotated horizontally on its axis so that the media cascade which results in the grinding action. The ceramic particles move between the much larger media and between the media and the wall of the mill and are broken into smaller particles. Operating variables include the size and angular velocity of the mill, the size of the media relative to the size of the feed material, the loading of the mill, the relative volumes of media and feed material, the physical characteristics of the media, agglomeration of feed or product, and in wet milling, the viscosity of the slurry during milling [22, 23].

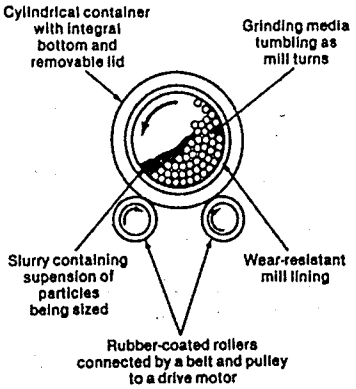

Figure 5.2. Schematic cross section showing the key elements of a typical ball mill [22]

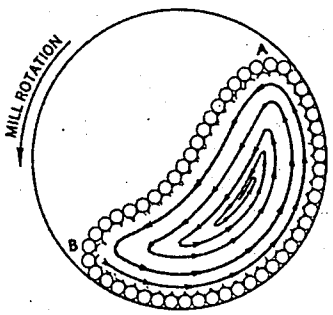

Figure 5.3. Schematic diagram of a ball mill showing cascading from A to B and subsequent media movement [23]

The effective angular velocity of the ball mill has a critical range. At low velocities the grinding media simply roll over the material to be ground without having any grinding effect. At high angular velocities the grinding media are trapped at the walls of the container due to the centrifugal forces arising from the rolling of the cylinder.

High-specific-gravity media can accomplish a specified size reduction much more quickly than low-specific-gravity media. Therefore; WC, steel, ZrO_2, Al_2O_3 and SiO_2 are commonly used in ball milling [22].

Initial particle size reduction is rapid but decreases as the powder becomes finer. Finally, ball milling produces a broad particle size distribution reducing the average particle size to 5 μm or less [22].

Contamination is a problem in milling; while particle size is being decreased, the mill walls and media are also wearing. To control contamination mill lining and the media should be carefully selected. Very hard grinding media can reduce contamination because they wear more slowly [22].

Since contamination is unavoidable the only way for zero contamination is using grinding media of the same composition as the material being ground. In all other cases where media and powder are of different materials sedimentation, chemical leaching and magnetic separation techniques are used to remove contamination.

Milling can either be accomplished wet or dry. Each method has its own advantages and disadvantages.

Table 5.1. Comparison of the advantages of wet and dry ball milling [22]

Advantages of wet milling	
	Low power required
	No dust problems
	Higher rotational speed
	Can wet screen through fine screen
	Good homogenization
	Smaller particle size than dry
	Narrower particle size distribution than dry
	Compatible with spray drying and casting processes
Advantages of dry milling	
	Avoids drying of the powder
	Avoids reaction of the powder / liquid
	Less media and lining wear than wet
	Can be started / stopped any time
	Easier to optimize

Attrition milling is another method to obtain particle size reduction. An attrition mill, called an attritor in short, is similar to a ball mill in that it consists of a cylindrical container in which grinding balls similar to that used in ball mills and the material to be ground are put.

In a vibratory mill, the energy necessary for the particle size reduction process is supplied through vibratory motion of the container. Grinding media and the material to be ground are placed in a stationary container under the presence of a liquid and the container is set into vibrating motion from the bottom center of the mill.

Fluid energy mills achieve particle size reduction by particle-particle impact in a high-velocity fluid which can be compressed air, nitrogen, carbon dioxide, water or superheated steam. The powder is added to the compressed fluid and accelerated to sonic or near-sonic velocity through jets leading into the grinding chamber. The grinding chamber is designed to maximize particle-particle impact and minimize particle-wall impact [22].

5.2. Forces on the Particles in the Milling Operations

Milling operations produce compressive and shear loads on the particles simultaneously. Shear and tensile stresses are produced by in-line compressive loads, shear is also produced by rolling loads, and attrition is produced by frictional stresses. While falling or vibrating media produce a compressive in-line impact, shear is produced when a particle is seized between two surfaces moving with different velocities relative to each other. On the other hand, attrition is produced by sliding and rubbing of particles between hard surfaces.

In general, it can be said that the mean size of fracture fragments is smaller when the impact force is higher. However, the reduction ratio is dependent on the microstructure of the particles as well, meaning that microstructural defects which decrease the strength of a particle may increase the reduction ratio.

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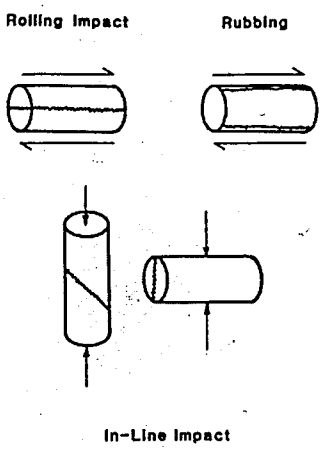


Figure 5.4. Shear stresses in particles are produced by rolling and rubbing actions, and shear and tensile stresses by compressive loading [23]

When large media are used a combination of in-line and rolling impacts act on the particles to be ground. The role of attrition can be increased by decreasing the media size and the impact force and increasing the frequency of rubbing contact stresses.

5.3. Milling Energy

The grinding energy is simply proportional to the mass and the change in velocity of the media during the impact:

$$\text{Energy} = \Delta\,(\tfrac{1}{2}\, m\, v^2)$$

where; m is the mass of the media, and v is the velocity of the media.

Increasing m directly increases the energy on impact. For this purposes either media of larger size or greater density can be chosen.

Media having a high elastic modulus produce a greater dv/dt. The grinding media must also be hard, fine-grained and nonporous to resist abrasive wear [23].

Viscous flow and elastic deformation are factors reducing the stresses in grinding operations. Since the dv/dt is reduced by the anelastic deformation, the impact load on

the particle is lower when grinding an anelastic material, e.g. deformable dense materials and porous agglomerates and aggregates.

Agglomerates absorb some of the impact energy and reduce the energy for particle fracture. Packing of agglomerates on the mill lining can isolate particles from the milling process. To overcome this problem, surfactants like alcohols, oleic acid, glycols or silicones can be used in small amounts, usually less than 1 % is sufficient to minimize agglomeration and packing. In wet milling, a deflocculent is used to disperse agglomerates. At this point the choice of the deflocculent is important since it should not degrade during milling. Again in wet milling, water or other chemical materials may be adsorbed in cracks and reduce the strength of the material, thus aiding grinding.

5.4. Milling Performance and Efficiency

The efficiency of communition equipment can be better understood by considering the following equality [23]:

$$\frac{\frac{Particles}{generated}}{Time} = \frac{Media}{collisions} \frac{Particle}{impacts} \frac{Particles}{Collision} \frac{}{Impact}$$

In order to better to understand the effect of terms on the right hand side of the above equation each of them must be separately interpreted.

The amount of particles generated in a given period of time is directly related to the number of fractures. The number of fractures increases when the frequency of collisions is higher, which increases with a decrease in the size of the media and an increase in the velocity of the media.

The probability of an impact increases with increasing concentration of particles on the surface of the media and with decreasing particle size. The uniformity of the particle size distribution also increases the impact probability. Agglomeration decreases

the impact frequency. Therefore the slurry viscosity should be enough to reduce the mobility of the particles and maintain uniform coating on the media and retain particles in the impact region.

The fracture probability increases when the grinding stress is large and the strength of the particles is low. Agglomeration may disperse on impact but absorb energy needed for grinding whereas collision forces are dissipated when the slurry viscosity at the shear rate of milling is too high. In general, the reduction ratio decreases as the particle size becomes smaller.

Thus to conclude, any grinding action which increases the frequency and energy of the collisions increases the rate of milling, in general. For efficient milling, the slurry should be deflocculated to disperse agglomerates. Otherwise, the rate of size reduction decreases. This is again the case as the particles become finer and finer. To avoid this, the solid content of the slurry may be increased to develop a coating on the media which also minimizes media wear and slurry contamination.

5.5. Milling Practice

The critical angular frequency of a ball mill causing centrifuging is [23]:

$$\omega = \frac{1}{2\sqrt{R}}$$

where; ω is the critical angular frequency in Hz and R is the radius in meters of the ball mill.

Adhesion resulting from the viscosity of the slurry reduces the critical value of ω leading to a practical operation range of 0.65 to 0.85 of the critical value of ω.

In practice, the media charge can be set to 50 % of the volume of the mill and powder or the slurry is added to slightly exceed the void spaces in the media. This combination promises a good compromise between the milling efficiency and the wear

of milling media and lining. Another rule of thumb used in laboratory scale applications is filling setting the media and the powder volume equal to one third of the total volume of the mill. The remaining one third is filled with an appropriate medium like air, an inert gas, water or another liquid. Both approaches can lead to satisfying results. For particular applications or for certain results, the media and the powder volume can be adjusted according to the remarks stated.

The wear resistance of the media and lining should be matched. For this purpose, it is of general practice that similar media and mill lining are used in a single application. However, it is not impossible to use a mill lining that is easy to wear out, like plastics, with a hard-to-wear media and to remove contamination from the mill lining with certain techniques.

Smaller media charges and higher material loading are often preferred for agglomeration dispersing and slurry mixing purposes. To minimize contamination and to grind though materials wear-resistant media should be considered. Media size must be kept uniform unless an application requires it otherwise since media of mixed size may wear more rapidly generating more contamination. A higher viscosity of the slurry requires a higher-density or larger media.

5.6. Communition Additives

During milling and grinding operations particles stick together due to surface forces which results in agglomerates of the existing powder. These effects the flowing capability of the powder in case of dry milling and the viscosity of the slurries in wet milling and decrease the efficiency of the milling and grinding operations. In order to prevent this the slurries must be kept free-flowing. This is accomplished by the use of chemical additives, called deflocculants, during the communition processes.

In case of dry milling the powder must be kept free-flowing. For this purpose dry lubricants such as stearic acid, oleic acid, zinc stearate, ammonium stearate, ethylene glycol, triethanolamine, glycerine or naphthenic acid can be used in very small amounts

such as 0.5 to 1 weight %. The surface coating effect of the dry lubricant increases the flowing capability of the ceramic powders [22].

In case of wet milling deflocculants are used to increase the flowing capability of the slurry. Deflocculants are chemical substances absorbed on the particles. These cause dispersion which increases the repulsive forces by electrical charging and / or sterically hindering the close approach of particles [23].

A very small amount of deflocculant can have a very significant effect on the end results of the communition process. Deflocculants can be applied from 0.5 to 2 wt. % regarding to their characteristics and to the conditions. However, addition of 1 w. % deflocculant is common and greatly effects the dispersion of the slurry.

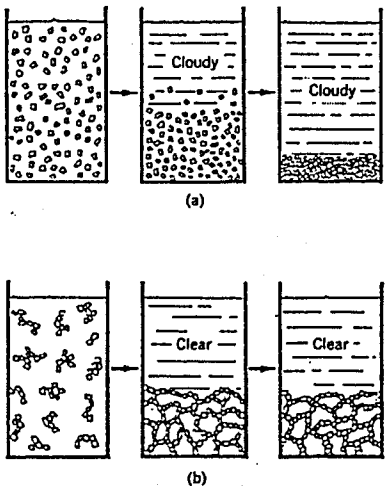


Figure 5.5. Sedimentation behavior for (a) deflocculated and (b) coagulated suspensions [23]

The dispersion of ceramic particles in a fluid is affected by the electrical potential at the particle surface, adsorbed ions, and the distribution of ions in the fluid adjacent to the particle. Electrostatic repulsion involves the buildup of charges of the same polarity on all particles. Like charges repel, so the particles are held apart in the suspension of the particles. The higher the electrical charge at the surface of the particles, the better the degree of dispersion and the less agglomeration. The charge at the surface of

particles is controlled by pH of the liquid and by addition of chemicals that supply monovalent cations (Na^+, NH_4^+, Li^+) for adsorption at the surface of the particles [22].

Another way to avoid agglomeration involves the addition chainlike organic molecules that are adsorbed onto the ceramic particles and provide a buffer zone around each particle. One end of the chain attaches or anchors to the ceramic and has limited solubility in the solvent whereas the other end extends away from the particle and is soluble in the solvent. The affinity of one end of a chain molecule to be adsorbed at the surface of the ceramic particle, the resistance of the tail end of the molecule to attach to the ends of adjacent molecule tails, the characteristics of the fluid and the length of the organic molecule are factors influencing steric hindrance [22].

Table 5.2. Common deflocculants used in water [23]

Inorganic	Organic
Sodium carbonate	Sodium polyacrylate
Sodium silicate	Sodium citrate
Sodium borate	Sodium succinate
Tetrasodium pyrophosphate	Sodium tartrate
	Sodium polysulfonate
	Ammonium polyacrylate
	Ammonium polysulfonate

According to the related literature, other deflocculants used for dispersion are ammonium polymethacrylate, ammonium polycarbonate and ammonium polycarboxylate.

5.7. Wet Ball Milling of Hydroxyapatite Powder

Wet ball milling is a suitable method to break the agglomerates of the hydroxyapatite powder and to decrease the size of the existing particles. There are numerous applications of ball milling of hydroxyapatite in the literature in which milling bowls and grinding media of different size and material are used. Since

hydroxyapatite is a moderate ceramic material regarding the hardness located almost in the middle of the Moh's Scale milling of hydroxyapatite is relatively simple compared to other harder ceramics. Accordingly, bowl and grinding medium alumina and zirconia, especially yttria-stabilized-zirconia, are satisfactory candidates. Preferred milling liquids are water, ethanol and acetone. However, use of water eliminates the problem of controlling the pH of the medium due to the solubility of hydroxyapatite in acidic solutions.

It is stated in the literature that long milling times, high ball-to-powder ratios and bigger grinding balls lead to better milling results [28]. However, hydroxyapatite's moderate hardness can lead to the problem of wear of the bowl and media in case of improper choices of milling bowl and media and under long milling times. Therefore, milling should be done in a hard bowl using hard grinding media in relatively short times to avoid any impurities. On the other hand, long milling times do not only lead to impurities originating from the bowl and media but also cause production of ionic species due to dissolution. These ionic species can interact with the dispersing agent reducing its effectiveness [29].

Use of the dispersing agent is necessary to a great extent due to the hydrophillic nature of hydroxyapatite. Various dispersants applied in ball milling of hydroxyapatite in literature are known under the brand name Dispex A40, Tripoli Na, Dolapix CE, Targon 1128 and Duramax 3005, Tiron and Davran C. Among those polymethylmethacrylate and ammonium polycarbonate are the most commonly used ones [29-31].

6. PRESSING

Pressing is the simultaneous compaction and shaping of a powder or granular material confined in a rigid die or a flexible mold [23]. For this purpose, free-flowing powder is placed into a die and pressure is applied to achieve compaction [22]. The free-flowing capability of the powder is obtained through the addition of binders and lubricants and a preconsolidation step.

There are two types of pressing, namely; uniaxial and isostatic. As its name implies in uniaxial pressing the pressure leading to compaction is applied in only one dimension which is the axial direction of the movement of the punch and die assembly. On the other hand, in isostatic pressing the compaction pressure is applied three-dimensionally by applying the pressure to a liquid which transfers this pressure to the part to be pressed. By the nature of the fluids the externally applied pressure on the fluid is applied in three dimensions to the part by the fluid.

6.1. Uniaxial Pressing

Most of the uniaxial presses are mechanical or hydraulic where the mechanical ones usually have higher production rates and are easily to automate.

In uniaxial pressing, the feed shoe fills the cavity with free-flowing powder mixed together with the necessary binders and lubricant and contains the required amount of moisture, while retracting the feed shoe smoothes the powder surface as it passes. Following this the upper punch moves down to precompress the powder. Then, both the upper and the lower punches simultaneously compress the powder while moving independently to their preset positions. The upper punch retracts and the lower punch continues its motion in the upper direction, finally ejecting the compact from the die body. The feed shoe moves then into its position to fill the die with powder for the next cycle. During its motion it also pushes the compact away from the punches. At the same time, the upper and lower punches return back to their initial positions.

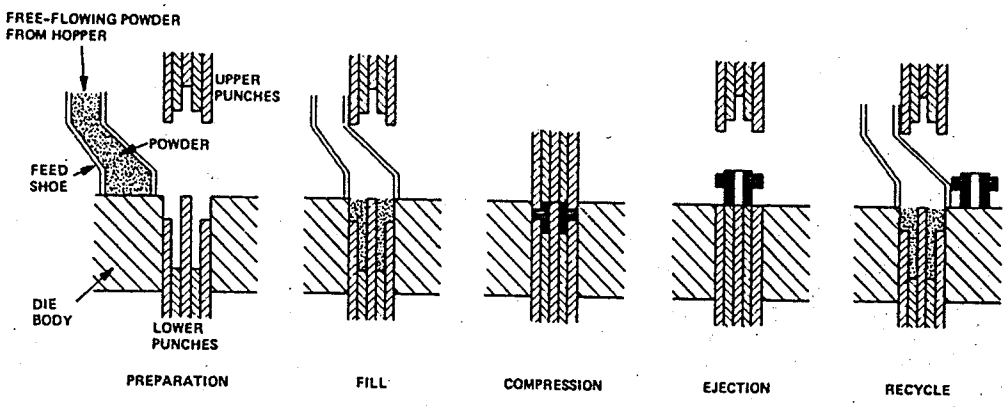


Figure 6.1. Schematic illustrating automated uniaxial pressing [22]

The described cycle can be repeated 6 to 100 times per minute depending on the specifications of the press and the part being fabricated [22]. Presses of operating capacity of 1 to 20 tons are common whereas special designs can reach up to 100 tons.

6.2. Dry vs. Wet Pressing

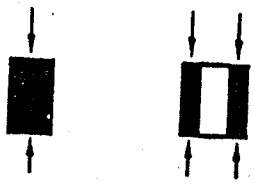
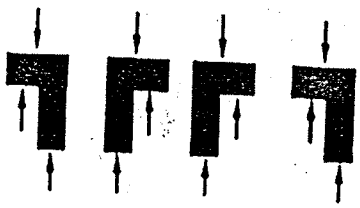
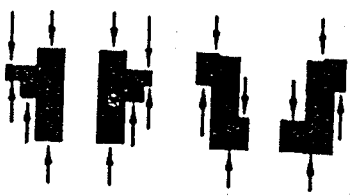
In dry pressing granulated or spray-dried powder with 0 to 4 % moisture is compacted to the desired shape. During the compaction process the granules are crushed and the particles are mechanically redistributed into a closed-packed array. A lubricant and a binder are usually added to the powder before the compaction which aid in the redistribution. The binder also provides cohesion. To achieve the crushing of the granules and uniform compaction of the powder normally high pressures are applied. Usually, dimensional tolerances are at the level of ± 1 % and can be decreased for specific applications.

Wet pressing involves a feed powder containing 10 to 15 % moisture. This type of pressing is usually used for clay-containing compositions. Wet feed powder can easily deform plastically during pressing and conform to the contour of the die cavity. Pressed shapes usually contain thin sheets of material at the edges where the material extruded between the die parts and can deform after pressing if not handled carefully. This makes wet pressing not well-suitable for automation. Except this, the tolerance limits are usually only about ± 2 %.

6.3. Die Selection

The type of press and tooling selected is based on the size and shape of the parts to be pressed which are divided into classes.

Table 6.1. Uniaxial pressing part and tool specifications [22]

Class	Definition	Type of tooling	Typical part cross sections
I	Thin, one-level parts can be pressed from one direction	Single action	
II	Thick, one-level parts that require pressing force from both ends	Double action	
III	Two-level parts that require pressing force from both ends	Double action, multiple motion	
IV	Multiple-level parts that require pressing force from both ends	Double action, multiple motion	

Parts with a constant thickness and thin cross section can be succesfully pressed with single-action. However, with increasing thickness parts do not achieve uniform compaction if only pressed from one end. As a result of this double-action presses are required. Parts having complicated shapes with variations in cross-sectional thickness require an independent punch for each level of thickness.

Table 6.2. Dry-press modes [23]

Type	Die	Top Punch	Bottom Punch
Single action	Fixed	Motion	Fixed
Double action	Fixed	Motion	Motion
Floating die	Moves	Motion	Fixed

Dies and punches are usually made of hardened steel. However, specific conditions can require the use of special steel, carbide or ceramics. The distance between the die and the punch is usually chosen as 100 μm but if the powder to be pressed is microns-size than the die-punch clearance is chosen as a lower value such as 10 to 25 μm. Sometimes the die wall is tapered to ease ejection. The taper angle is usually less than 10 μm/cm.

6.4. Selection of Proper Compaction Additives: Binders and Lubricants

Binders and lubricants are widely used as compaction additives and play an important role in the properties and quality of the pressed part. Binders provide lubrication up to a certain extent but their primary role is giving the pressed part strength for handling, machining and end use. On the other hand, lubricants reduce the frictional forces between the particles and the particles and the die wall. Through the combined use of binders and lubricants the powder particles are made to slide past each other to rearrange in the closest possible packing and the interparticle and the particle-die wall friction is minimized to allow all portions of the compacted powder receive equivalent pressure.

6.4.1. Binders

In principle, the substance used as binder coats the surface of the particles to be compacted. This coating reduces the friction between the particles and acts as a partial lubrication. However, binder's primary objective is, as their name implies, to form temporary bonds after pressing. In this way, the compressed part can be taken out of the die without damage and the pressed part can be handled and machined safely. Usually,

use of very small amount of binders such as 0.5 to 5 % is sufficient to obtain the desired effect.

Binders can be classified as organic and inorganic depending on their chemical composition. As expected, organic binders decompose under high temperatures during the sintering stage and evolves gases. Some organic binders can leave a carbon residue during decomposition, especially if the sintering is done under reducing atmosphere. Alternatively, inorganic binders can be used. However, inorganic binders do not decompose during firing and remain totally in the compacted powder becoming part of it.

Another classification of binders is as being soft and hard. Soft binders such as waxes and gums are sensitive to temperature variations and they do not require moisture and addition of a further lubricant. However, they should be used with care to avoid changes in granule size since this may affect the flow characteristics in a negative manner or cause inhomogenous density distribution in the compact. A possible danger of using soft binders arises in their sticking tendency which can alter the properties of the end part and can decrease production rate.

Hard binders have the advantage of producing hard granules which are dimensionally stable and free flowing. However, since these hard granules are not self lubricated use of a proper lubricant and some moisture is necessary upon the usage of a hard binder. In addition to this, the presence of the hard granules requires the application of higher pressures to break the hard and though granules which can limit the strength of the final part.

Accordingly, waxes and gums are soft binders whereas dextrin, starches, lignins and acrylates are hard ones. Polyvinyl alcohol and methyl cellulose are somewhat in between.

The hardness and deformation characteristics of binders depend on several parameters such as temperature and humidity and can be altered by the presence of other chemicals called plasticizers.

Many of the binders have a ductile-to-brittle transition characteristic. Below the transition temperature, sometimes called the glass transition temperature (T_g) they behave in a brittle fashion whereas they behave in a ductile manner above T_g. In the brittle region the deformation is primarily elastic, the total deformation is low and is completely recoverable after the removal of the load. However, such a behavior provides almost no binding effect on the compact. On the other hand, in the ductile region, which lies above the glass transition temperature, the deformation is primarily plastic and it is large which is a desired property for a binder.

Plasticizers effect the ductile-to-brittle characteristics of the binders rendering them as ductile in the temperature range in which the pressing process is conducted at. Different chemicals act as plasticizer for different binders. A widely used binder-plasticizer set composes of polyvinyl alcohol as binders and polyethylene glycol as plasticizer which reduces the transition temperature of polyvinyl alcohol and makes it ductile, thus suitable to be used as a binder, at room temperatures.

6.4.2. Lubricants

Lubricants are materials with low shear strength. As their name implies, they are used to reduce the friction present in every form during the pressing process. Hence, they minimize the friction between the particles, between the granules and the powder and the die-wall. This is very important for the increase and uniformity of the density and reduction of shrinkage during sintering of the pressed part. Their use also increases tool life by minimizing wear which also decreases impurities on the surface of the pressed part. By avoiding frictional forces the pressing force and the force necessary for ejection can also be decreased without any loss in the final properties of the compact.

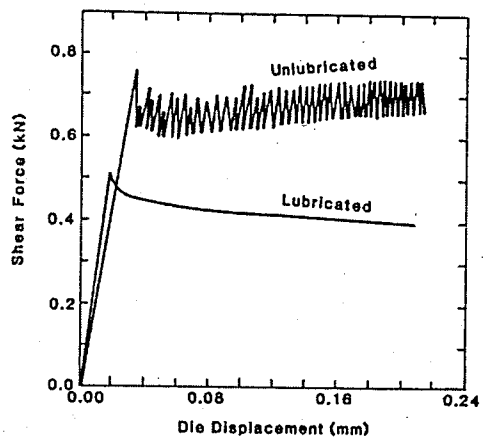


Figure 6.2. Regular and slip-stick shear produced on displacing the die while the compact is compressed [23]

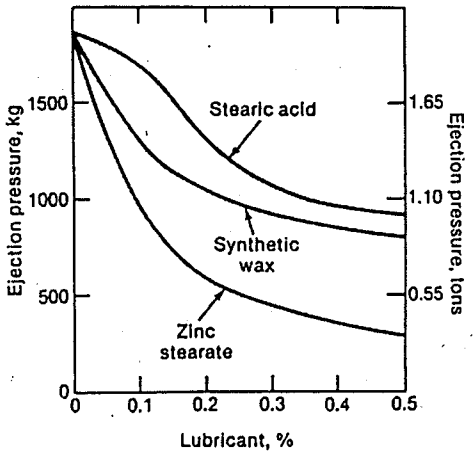


Figure 6.3. Effects of lubricants on decreasing die-wall friction and the pressure to eject a pressed part from a die [22].

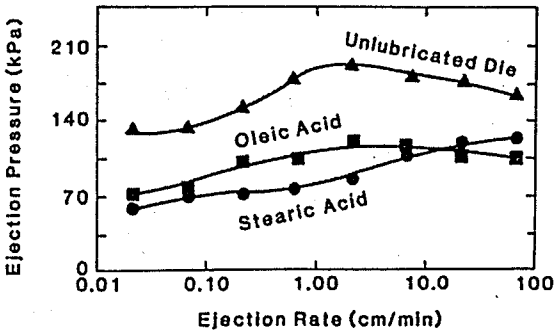


Figure 6.4. Effect of lubrication on ejection pressure for an alumina compact with a polyvinyl alcohol binder (23 °C) [23]

Very small amounts of lubricants, such as 0.5 to 2 %, are sufficient to obtain the desired effect of reducing the pressing and ejection force by several times as indicated in the above figures.

Zinc stearate, lithium stearate, potassium stearate, sodium stearate, ammonium stearate, magnesium stearate, stearic acid, naphthenic acid, oleic acid, boric acid, (hexagonal) boron nitride, oils, graphite, paraffin, synthetic wax and talc are commonly used as lubricants in pressing operations.

6.5. Compaction Process

Initially, the rate of compaction is high during the compaction process but above 5 to 10 MPa the rate rapidly decreases. The initial stress is transmitted by means of contacts between particles coated with the binder system [23].

The particles in the granules slide and rearrange leading to the deformation of the granules which further leads to a reduction in the porosity and an increase in the amount of intergranular contacts. During this air found in compressed state in the pores migrate and exhausts between the punch and die assembly, to a certain extent.

Since the overall volume occupied by the powder during the compaction process is reduced through the motion of the punch in the die while the total mass of the powder is unchanged the compaction process decreases the overall density of the compacted powder.

To get a deep but simple understanding about the applied compaction process a ratio is defined as Compaction Ratio = Pressed Density / Fill Density. Commonly, the compaction ratio is less than 2 for many applications and for most of the ceramic materials. Particularly, powders composed of ductile particles such as metal powders can have a higher compaction ratio than this.

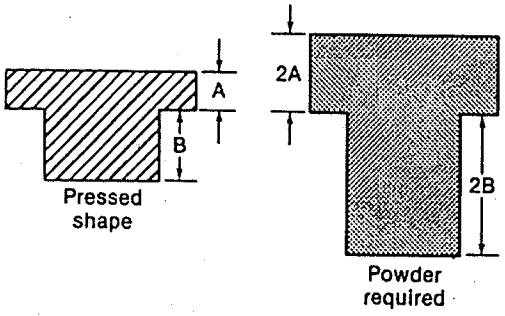


Figure 6.5. Schematic illustrating the different distances a punch must move to accomplish uniform compaction of the powder. Based on a powder with a compaction ratio of 2:1 [22]

To get a deeper insight the compaction process can be separated into three stages. These can be differentiated by the dependence of the compact density on punch pressure.

In the first stage a slight densification occurs due to the sliding and the rearrangement of the granules. In this stage, the interstices among the granules are still much larger than the average pores within granules.

In the following stage, the volume of the relatively large interstices reduces due to the deformation and fracture of the granules and interfaces between smaller and softer granules begin to be eliminated. In this stage, the apparent yield pressure of the granules is less than 1 MPa in the case of a soft and ductile binder system. However, if the binder system is poorly plasticized or some of the granules have reached a higher binder content the needed pressure increases to obtain the desired compaction. This, in turn, shows the importance of choosing the correct binder amount and mixing the binder thoroughly with the powder.

In the last stage, most of the large pores among deformed granules have already disappeared. Further, the particle in the granules slide and rearrange due to the high pressure and interstices between large granules or harder granules and within large granules are eliminated.

The below figure clarifies the three stages of compaction.

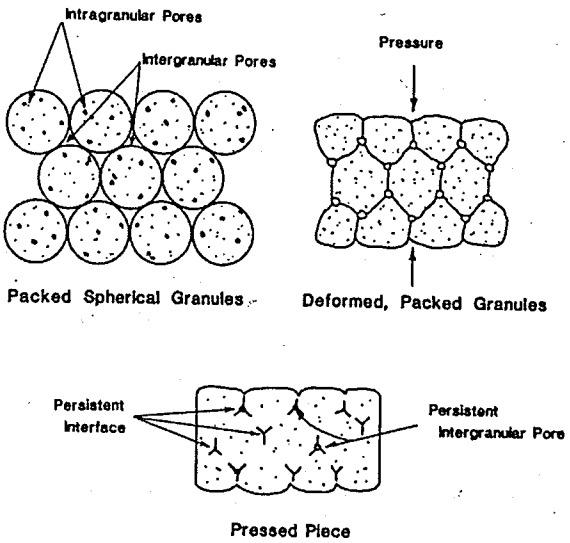


Figure 6.6. Change in granule shape and bimodal pore size distribution during compaction [23]

6.6. Stress Considerations in Uniaxial Pressing

A portion of the applied load is transferred to the die wall during compaction which produces a friction between the die wall and the compact. This frictional force results in pressure gradients in the compact which further cause density gradients in the final pressed part.

The shear stress on the die wall which increases by increasing pressure can succesfully be reduced by proper lubrication. The die wall stress is also high for a low yield strength of the granules and a low pressing speed. These can be summarized in the following equation [23]:

$$\bar{\tau}_W = fK_{h/v}\overline{P} + A_W$$

where; $\bar{\tau}$: Mean shear stress at the die wall

f : Coefficient of friction

$K_{h/v}$: Horizontal/vertical stress ratio parameter

$\overline{P}$: Mean axial pressure

Aw : Adhesion at the die wall.

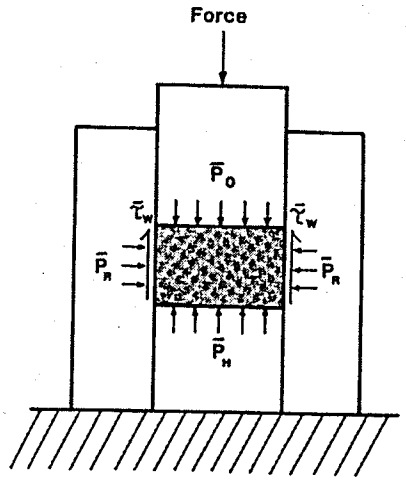


Figure 6.7. Mean stresses on the compact during unidirectional compaction [23]

Regarding the axial pressure transmission through the compact it is stated that [23]:

$$\frac{\overline{P}_H}{\overline{P}_a} = \exp\left(\frac{-4fK_{h/v}H}{D}\right)$$

where; $\overline{P}_H$: Pressure at depth H

$\overline{P}_a$: Mean applied pressure

f : Coefficient of friction

$K_{h/v}$: Horizontal/vertical stress ratio parameter

H : Depth

D : Diameter

The axial displacement is greater in the center of the compact than near the die wall during pressing. This is obvious due to the die wall friction. The average movement of the particles decreases at a greater distance from the moving punch. There

is also some amount of radial translation where the slippage is inclined relative to the axial direction.

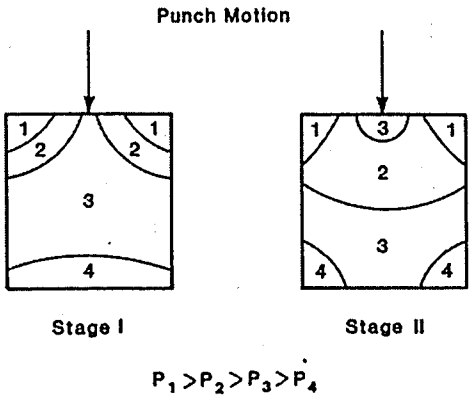


Figure 6.8. General pressure profiles for unidirectional pressing [23]

As seen in the above figure, maximum pressure occurs near the top edge whereas minimum pressure areas are in depth towards the central axis. The below figure gives in depth information for pressure variations for different length-to-diameter ratios of the pressed part.

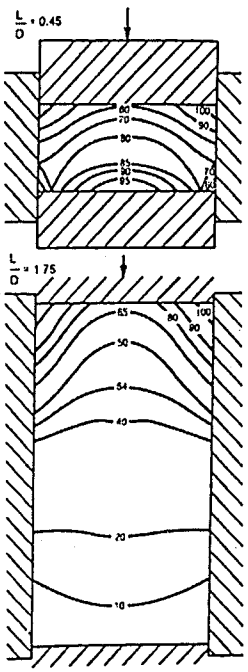


Figure 6.9. Pressure variations in uniaxial pressing due to die-wall friction and particle-particle friction, which lead to nonuniform density of the pressed compact [22]

6.7. Removal of the Pressed Part

During pressing, elastic compression of the granules begins in the second stage and increases in the third stage after which the part is removed from the die. An unwanted increase of the dimensions of the pressed part can occur while ejection which is a consequence of the stored energy during the compression. This is called springback.

A small springback, which is usually desired to be amount 0.75 %, is necessary to cause the compact to separate from the punch. However, a larger springback due to stress gradients may result in defects on ejection from the die.

An additive such as gum arabic which increases moisture adsorption increases the plasticity of the binder system which in turn reduces the springback at lower humidity. However, care must be taken at higher moisture contents since the presence of gum arabic can cause further springback due to its larger molecular size. Springback is also a significant problem at higher compaction pressures.

The ejection process from the die depends on the taper and surface conditions of the die, elastic springback of the pressed part, lubrication between the die wall and the part and the rate of ejection.

Appropriate selection of a binder can reduce the ejection pressure by a factor of 5 to 10. A further reduction can be obtained by a properly selected die wall lubricant. Lubrication is not only important for the ease of ejection but it also reduces die wear.

6.8. Problems Encountered in the Pressed Parts after Uniaxial Pressing

- Usually, there are four different types of problems which can be encountered in uniaxial pressing. These are improper size, improper density, density variation, and cracking (end and ring capping) and lamination [22, 23].

Improper size and density are problems which are relatively simple to detect. They are usually a result of batches which are out of specifications. Hence, they can be easily eliminated by controlling the process and by improving quality control.

Density variations, and the resulting nonuniform density, can result in cracking during firing. This can either be caused by the friction between the compacted powder and the die wall, presence of hard agglomerates or improper filling of the die.

The friction arises from the particle-particle and particle-die wall interactions. As a result, uniaxial pressure applied by the punch dissipates because of the friction such that particles near the die wall experience a lower pressure than the particle in the middle of the compact which are far away from the die wall. Followingly, the areas experiencing lower pressure will compact less, meaning a lower density, and the areas experiencing higher pressure will compact more, meaning a higher density. Finally, during the firing process, the lower density areas will either not densify completely or will shrink more than surrounding areas. The pressure difference between the middle and circumferential parts of a compact increases as the length-to-diameter ratio increases.

Powder which is stacked improperly in the die will compact to different densities, and hence, to different porosities during pressing. The regions of decreased porosity will shrink less and the regions with increased porosity will shrink more leading to distortion of the pressed part.

Also hard agglomerates can be a source of nonuniform density distribution by shielding the softer surrounding powder from the applied pressure. This can result in build-up of pore groups which will decrease the strength of the part. In other cases, the agglomerate itself can be an entrapment for porosity and during firing, the agglomerate densifies more than the surrounding material leaving a large pore behind.

Finally, powder which is nonuniformly stacked in the die will not be able to reposition during pressing. The regions with higher green density will consequently

compact to a higher density in the final compact. Since the regions of decreased porosity will shrink less in this way, distortion will be possible to occur in the final part.

The last of the problems, namely cracking and lamination, may be due to improper design of the die, pressure gradients in the compact resulting due to die-wall friction, stored elastic energy gradients due to nonuniform granules, nonuniform filling or entrapped air, rough surface of the die wall due to wear, or rebound during ejection.

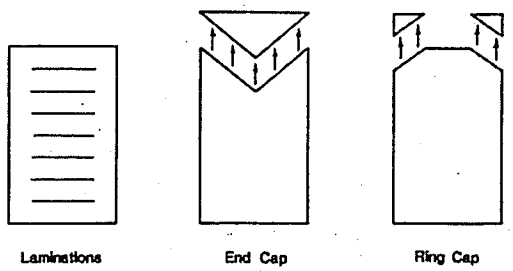


Figure 6.10. Common defects in pressed compacts [23]

The comparison of the above figures clearly shows the effect of the pressure ingredients during the compaction on the defects of the final part.

Laminations near edges are often produced by the wedging of powder between the punch and die wall when the gap is too large relative to the minimum granule size. The probability of lamination to occur can be decreased by reducing the average springback, changing the composition of the powder to increase the compact strength, reducing the pressing pressure or lubricating the die to decrease pressure gradients, and using a die of sufficient stiffness with a smooth wall and entry bevel.

End capping can occur because of springback while releasing pressure from the punch. A tensile stress concentrated at the upper edge of the compact develops since material rebounds near the top center of the compact, but it is restricted at the edges due to frictional drag between the compact and the die-wall. Minimizing the die-wall friction by the use of a lubricant, increasing the strength of the compact through the use of a proper binder, minimizing rebound and maintaining hold-down pressure on the upper punch can greatly reduce the tendency for end capping.

Ring capping can occur during ejection while the material rebounds to a larger cross section which introduces a tensile stress to the material above the top of the die. A good binder selection can reduce ring capping possibility.

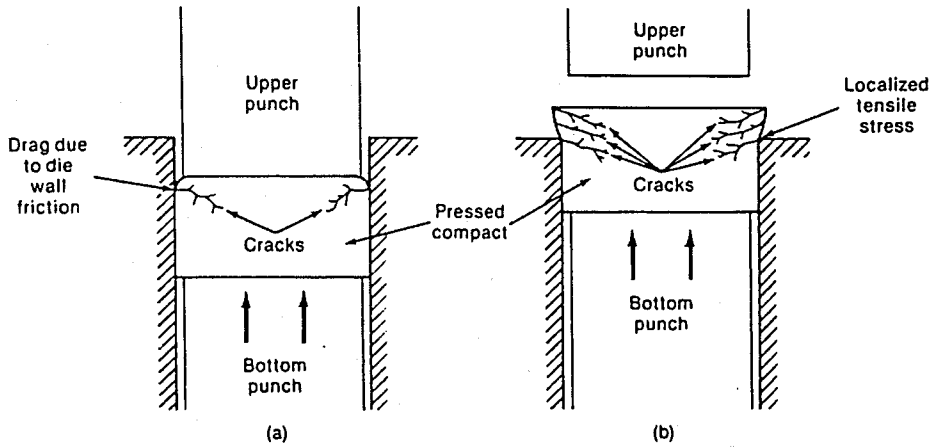


Figure 6.11. Mechanism of formation of laminar cracks in uniaxially pressed parts.
(a) Pressure being released from upper punch and
(b) Material rebound at top of die [22]

Entrapped air in pores can also lead to cracks when the compaction ratio and velocity are high and the thickness of the compact is relatively large.

Low gas permeability and low strength of the compact increases the tendency to these types of cracks.

6.9. Pressing of Fine Hydroxyapatite Powder

According to the literature, pressing of hydroxyapatite prior to sintering is conducted at pressures varying from 10 to 390 MPa.

Tas *et al.* [32] has found that the synthetic hydroxyapatite pellets pressed at 390 MPa and sintered at 1200 °C for 10 hours could gain 99 % of the theoretical density.

Gibson *et al.* [33] states that the sintered density of hydroxyapatite pressed at 30 MPa is 64 % of the theoretical density whereas it reaches a maximum of 92 % for samples pressed at 200 MPa.

Gokbayrak has presented in his study that samples pressed at pressures below 200 MPa did not acquire adequate strengths. So he has experimented higher pressures reaching up to 500 MPa and has found out that such high pressures in turn have resulted in defected bodies. He was able to produce undefected bodies which are mechanically of sufficient strengths at a pressing pressure of 350 MPa.

7. SINTERING

Compacted powders, called "green products", are fired in a furnace to develop desired microstructure leading to desired properties. Firing is a heat-treatment process which consists of three consecutive stages which are respectively: presintering, sintering, and cooling.

Table 7.1. Overview of the firing process including stages of sintering

Stages of the Firing Process	Steps of the Elementary Stages
Presintering	
Sintering	Initial sintering
	Intermediate sintering
	Final sintering
Cooling	

During sintering consolidation of the compacted powder occurs which means that powder particles join each other to form an aggregate having a certain strength where the compacted powder shrinks and densifies.

Sintering begins when the temperature in the product exceeds one-half to two-thirds the melting temperature, which is sufficient to cause significant atomic diffusion for solid-state sintering or significant diffusion and viscous flow when a liquid phase is present or produced by a chemical reaction [23].

7.1. Firing Equipments

Compacted ceramics are fired in a furnace which is an enclosed chamber in which heat is produced. There are batch and continuous types of ceramic furnaces. A batch type furnace simply consists of a heating chamber with an opening through which the part to be fired is fed into the inner volume whereas continuous types can have more complicated designs which makes the feeding in and taking out of the parts easier and

faster. Various types of continuous type of ceramic furnaces such as shuttle, elevator, rotary, periodic, car-type tunnel, sled and roller hearth ceramic furnaces can be used for various applications depending on the dimensions of the fired parts, on their heating and cooling characteristics and amount of the fired parts. Heating of the products are commonly done by combustion of natural gas, fuel oil or by electric heating.

Refractory metal alloy heating elements are used for heating to about 1150 °C, silicon carbide to about 1550 °C, and molybdenum silicide rods for heating to 1650 °C in an oxidizing atmosphere. Molybdenum, tungsten, and graphite may be used for heating above 1700 °C in an inert or reducing atmosphere. Induction, microwave, and plasma heating have been investigated. Significant improvements in the temperature uniformity and thermal efficiency have been achieved by using a greater amount of high-performance refractory insulation of much lower thermal mass and thermal conductivity, and higher-strength kiln furniture of thinner construction; these innovations enable the volume of product/furniture to increase in a setting and a faster firing when the kiln furniture is rate limiting [23].

7.2. Presintering

Presintering stage is composed of reactions prior to sintering including burnout of additives such as deflocculants, binders and lubricants and removal of gaseous products resulting from the oxidation and decomposition.

Before the temperature necessary for the sintering process has been attained several material changes take place in the product, like drying, decomposition of the organic binders, vaporization of chemically combined water from the surfaces of the particles and from within organic phases containing water of crystallization, the pyrolysis of particulate organic materials introduced with the raw materials or as contamination during processing, changes in the oxidation stages of some transition metal and rare-earth ions, and the decomposition of carbonates, sulfates, and the like, introduced as additives or a constituent of the raw materials [23].

Initial heating during the presintering stage may remove any liquid after forming and drying the product and any moisture adsorbed from the atmosphere during transporting and setting. The amount of adsorption can be significant especially when a warm product with a high specific surface area is removed form the dryer but cools in moist air before the firing step such that adsorbed moisture may exist in the product even at temperatures exceeding 200 °C.

Burnout of the binder is very important in this stage and depends on the binder composition and structure of the binder material, the composition surrounding and in the pores of the product, and the rates of diffusion of the decomposition product gases and furnace gas through the product. Since the volume the gaseous products may be several hundred times larger than the volume of the compact the binder burnout is a critical step during the presintering stage.

Polyvinyl alcohol can have a decomposition range which starts at 150 °C and continues until the product reaches 500 °C whereas waxes and polyethylene glycols melt at a relatively lower temperature and vaporize over a narrower temperature range. Binders which decompose in a narrow temperature range can cause oxidation heating which leads to a rapid increase of the temperature inside the product. The ash content is higher for natural binders and binders containing metal ions. Refined binders such as polyvinyl alcohol and cellulose type of binders leave a few percent ash. The residue after burnout of synthetic polymerized glycols and acrylic binders is a fraction of 1 % [23].

The burnout process may cause a slight volume expansion for dry-pressed parts where the particles are in contact but a volume contraction for tape cast or injection molded parts where the particles are separated by the organic phase. The apparent burnout temperature for a thicker product is higher. Burnout is suppressed when the oxygen pressure in the furnace is reduced.

7.3. Sintering

The sintering process consists of three consecutive stages. These are initial sintering, intermediate sintering and, final sintering.

In the initial sintering stage adjacent particles rearrange by slightly moving and rotating to increase the number of contact points, and initial neck formation at the contact point between each particle occurs. Bonding is initiated at the points of contact where material transport can occur and where surface energy is maximum.

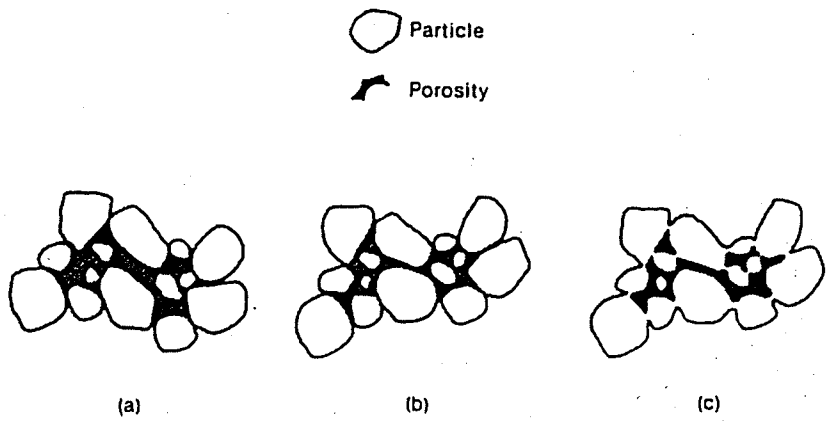


Figure 7.1. Changes that occur during the initial stage of sintering.
(a) starting particles, (b) rearrangement, and (c) neck formation [22]

During intermediate sintering the neck size between particles grows, porosity decreases and the centers of the original particles move close together resulting in shrinkage equivalent to the amount of porosity decrease. The grain boundaries begin to move so that one particle, called a grain, begins to grow while the adjacent grain is consumed allowing geometry changes which are necessary to accommodate further neck growth and removal of porosity. This stage continues as long as pore channels are interconnected and finishes when pores become isolated. Greatest part of the shrinkage during sintering occurs in this stage.

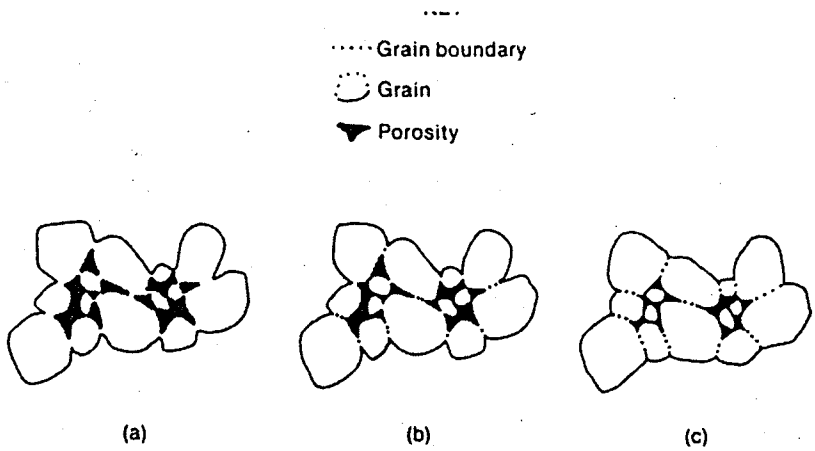


Figure 7.2. Changes that occur during the intermediate stage of sintering. (a) neck growth and volume shrinkage, (b) lengthening of grain boundaries, and (c) continued neck growth and grain boundary lengthening, volume shrinkage, and grain growth [22]

In the final sintering stage the final removal of porosity takes place by vacancy diffusion along grain boundaries which is aided by movement of grain boundaries and controlled grain growth. Grain growth must be controlled to obtain maximum removal of porosity since if the grain growth is too rapid the grain boundaries can move faster than the pores. In that case, the pores are left isolated inside a grain. During further growth of the grain the pore becomes more and more separated from the grain boundary. So the chance of eliminating the pore deceases.

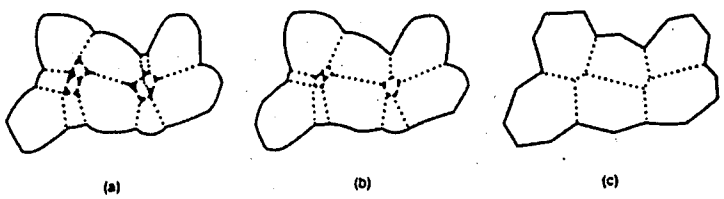


Figure 7.3. Changes that occur during the final stage of sintering. (a) grain growth with discontinuous pore phase, (b) grain growth with porosity reduction, and (c) grain growth with porosity [22]

7.4. Mechanisms of Sintering

Sintering takes place by a combination of different material, or mass, transport mechanisms some of which are can also result in densification.

Table 7.2. Mass transport mechanisms in sintering [23]

Mechanism	Densification
Surface diffusion	No
Boundary diffusion	Yes
Lattice diffusion	Yes
Viscous flow	Yes
Plastic flow	Yes
Evaporation-condensation	No

Surface diffusion is a general transport mechanism producing surface smoothing, particle joining, and pore rounding but does not cause volume shrinkage.

Diffusion along the grain boundaries and through the lattice of the grains produces neck growth and volume shrinkage.

Viscous and plastic flow mechanisms become important under the existence of a wetting fluid and an applied mechanical pressure.

7.5. Types of Sintering

The sintering process can be classified based on the types of the contributing mechanisms. In some types of sintering types a combined action of more than a single mechanism can take place.

Table 7.3. Sintering mechanisms [22]

Type of sintering	Material transport mechanism	Driving energy
Vapor-phase	Evaporation-condensation	Difference in vapor pressure
Liquid-phase	Viscous flow, diffusion	Capillary pressure, surface tension
Reactive liquid	Viscous flow, solution-precipitation	Capillary pressure, surface tension
Solid-state	Diffusion	Differences in free energy or chemical potential

7.5.1. Vapor-Phase Sintering

In this type of sintering material is transported from surface of particles to the contact region between particles. The smaller is the particle size the greater will be the driving force. Although vapor-phase sintering changes the shape of the pores and result in bonding between particles it does not produce shrinkage and therefore cannot produce any densification [22].

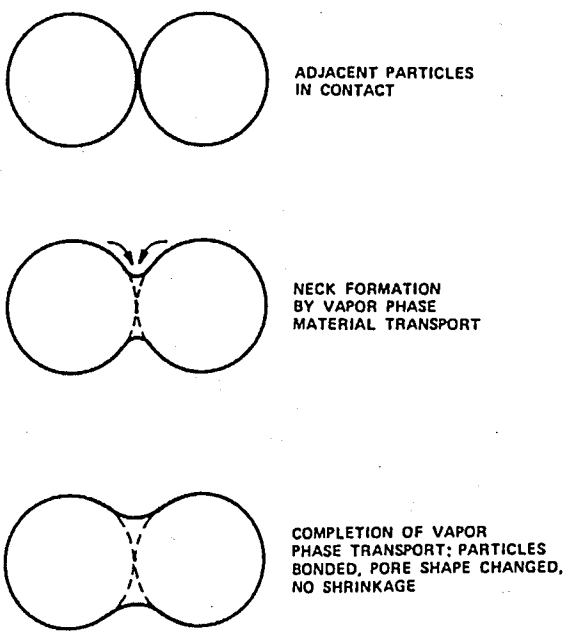


Figure 7.4. Schematic of vapor-phase material transport [22]

7.5.2. Liquid-Phase Sintering

In liquid-phase sintering a viscous fluid is present at the sintering temperature. This type of sintering is affected by the particle size, the viscosity of the liquid phase and the surface tension of which viscosity and surface tension are functions of the composition and temperature [22, 23].

With the liquid coating the grains, the material may often be sintered to a higher density at a lower temperature [22, 23].

The liquid between the particles rearrange the particles to achieve better packing and increases the contact pressure between particles, which increases the rate of material transport by solution and precipitation, creep and plastic deformation, vapor transport, and grain growth.

7.5.3. Reactive Liquid Sintering

This type of sintering is similar to liquid-phase sintering, however, the liquid either changes composition or disappears throughout the sintering process.

7.5.4. Solid-State Sintering

Solid-state sintering involves material transport due to volume diffusion which consists of the movement of atoms or vacancies along a surface or grain boundary or through the volume of the material.

Surface diffusion, like vapor-phase transport, does not result in shrinkage, whereas volume diffusion, whether along grain boundaries or through lattice dislocations, results in shrinkage [22].

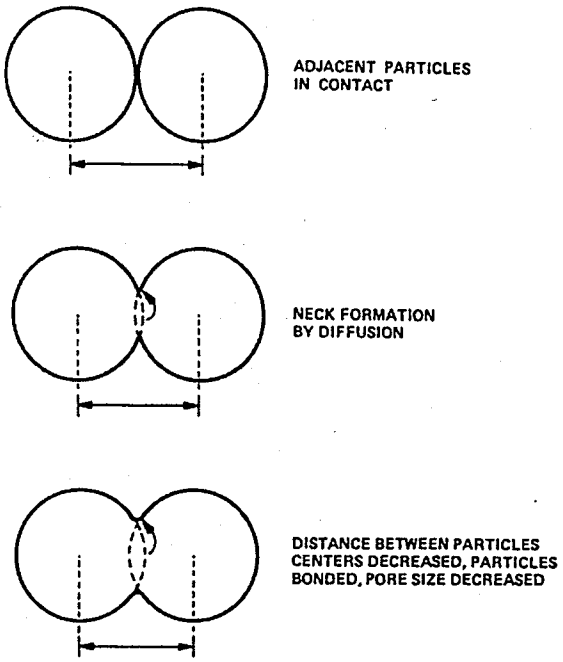


Figure 7.5. Schematic of solid-state material transport [22]

The driving force for solid-state sintering is the difference in free energy or chemical potential between the free surfaces or particles and the points of contact between adjacent particles. Accordingly [23],

$$\Delta G_T = \Delta G_v + \Delta G_b + \Delta G_s$$

where; ΔG_T : Total free energy of the system

ΔG_v : The change in free energy associated with the volume

ΔG_b : The change in free energy associated with the boundaries

ΔG_s : The change in free energy associated with the surfaces of the grains

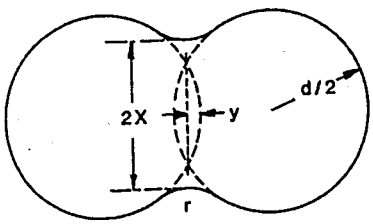


Figure 7.6. Two-sphere initial-stage sintering model [23]

The shrinkage of an interstice in a uniform packing of uniform crystalline spheres is considered as the model of solid-state sintering. Because of the chemical potential difference the concentration of vacancies beneath a concave surface is higher than beneath a flat or convex surface. The transport of vacancies from a concave surface can occur by the mechanisms of lattice and boundary diffusion, with a contaminant flow of atoms in the opposite direction. Neck growth occurs for boundary tension < $\sqrt{3}$ surface tension and the effect is pore rounding and a decrease in the total surface free energy according to [22]:

$$\cos\left(\frac{\phi}{2}\right) = \frac{\gamma_b}{2\gamma_s}$$

where; ϕ : angle of intersection of the pore at the pore-grain boundary juncture

γ_b : interfacial tension of the boundary

γ_s : surface tension

The general model of the material transport mechanism by lattice diffusion from the line of contact between two particles to the neck region sintering can be set up as follows [22, 23]:

$$\frac{\Delta L}{L_0} = \left(\frac{K\ D\ \gamma V t}{kTd^n}\right)^m$$

where; $\Delta L/L_0$: linear shrinkage (equivalent to the sintering rate)

K : constant dependent on geometry

D : self-diffusion coefficient

γ : surface energy

V : atomic volume of the diffusing vacancy

t : time

k : Boltzmann constant

T : temperature

d : particle diameter assuming equal-size starting particles

n : exponential factor, typically close to 3

m : exponential factor, generally between 0.3 and 0.5

The model works well for the initial stage of sintering. However, once the grain growth is initiated the model gets more complicated and the sintering gets dependent also on the shape and packing of particles because particle aggregates are a common source of packing heterogeneity and inhomogenous sintering.

A closer observation of the mathematical model reveals that the shrinkage is very temperature dependent since the diffusivity varies exponentially with the temperature ($e^{-Q/kT}$).

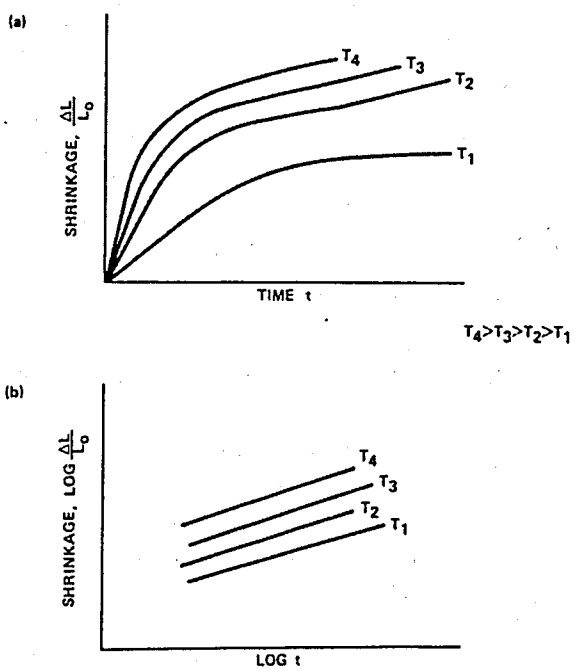


Figure 7.7. Typical sintering rate curves showing the effects of temperature and time [22]

Another important remark with respect to the mathematical model will be that smaller starting particles will result an equivalent shrinkage in a shorter time. So, milling of the powder prior to sintering stage turns out to be a very significant step

because it both decreases the particle size as well as enhances the particle size distribution.

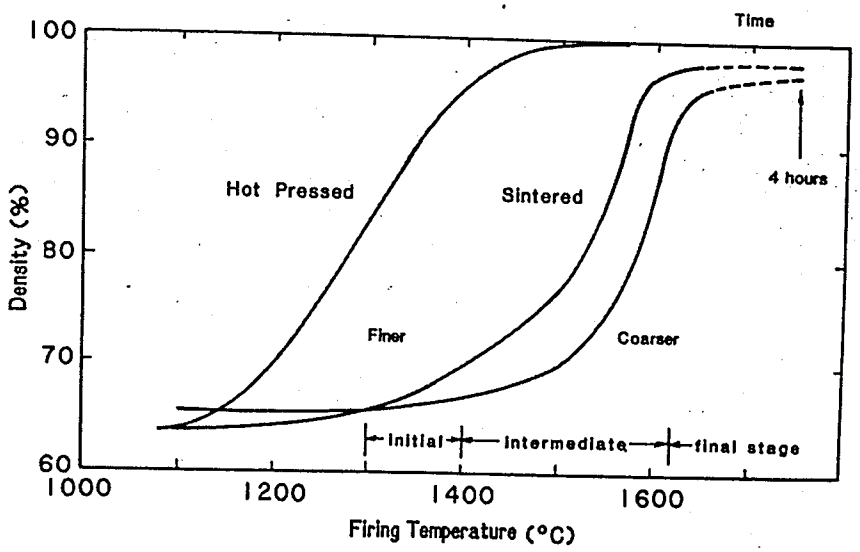


Figure 7.8. Densification behavior of compacts of two log-normal alumina powders ($\bar{a}_{gM}$ = 1.3 and 0.8 μm) and the initial, intermediate, and final stages of sintering for the coarser powder [23]

7.6. Cooling

Cooling stage contains thermal and chemical annealing of the part and is necessary for the removal of the enormous amount of heat from the fired part and to decrease its temperature to a low value which makes handling easier. This is usually the atmospheric or a slightly higher temperature at which removal of the part from the furnace and its transportation is made possible.

Cooling can be done very rapidly for ceramics which do not require thermal and chemical annealing where the cooling rate can be as high as the thermal shock resistance of the firing equipment allows. On the other hand, cooling must be done very slowly for thicker products with average thermal stability. Some special ceramics require cooling in an atmosphere which is different than the sintering atmosphere which

is necessary to change the oxidation state of component ions, alter the stoichiometry, or alter the phase equilibrium.

Behind the importance of the cooling stage lies the fact that stresses which are caused by differential thermal contraction during cooling may result in small cracks in the products or even lead to complete failure of the part. Tensile stresses may usually produce fine cracks whereas a high compressive stress may cause peeling.

7.7. Controlling the Sintering Process

Densification during sintering is effected by the composition, particle size distribution, temperature and time at temperature. Therefore, these factors must be controlled to control the whole sintering process.

In addition to these factors, also the atmosphere, time/temperature cycle, design and material of the furnace, and processing steps of the compacted powder before sintering play an important role in the sintering process.

Sintering conducted in air can lead to oxidation whereas a reducing atmosphere can lead to reduction. Residual binder can cause localized reducing conditions and cause sintering to be retarded or accelerated.

Time/temperature cycle includes factors like the rate of heating, peak temperature, the time at peak temperature, and the rate of cooling. Time at temperature and peak temperature effect the amount of total densification and the degree of grain growth whereas cooling rate effects the amount of residual glass in the sintered object. These in turn, effect the strength and toughness of the final product. An accelerated heating up or cooling down can lead to cracks due to thermal shock whereas a rapid heating up can also cause cracks due to the quick burning off of the binders and other organic additives.

7.8. Problems Encountered in Sintering

Some problems can occur during and after the sintering process. These are warpage, overfiring, problems related to the binder burn-off, the decomposition reactions and the polymorphic transformations.

Warpage is caused by improper support during sintering or from density variations. It is easier to correct the first by using special supporting apparatus. However, density variations are difficult to handle and must be corrected at earlier stages of production.

Overfiring can result in warpage, reaction with surrounding furnace structures, bloating, or excessive grain growth. An increase in grain size decreases the strength of the part.

Binders, which are mostly of organic nature, are added to the powder to be compacted before the sintering. Therefore, during sintering they can result in carbon residues. Especially in applications where large amounts of binder have to be used the binder removal must be very slow as a gas or liquid by thermal decomposition. Otherwise, cracks can occur in the product. In order to properly remove the binder the temperature is slowly raised to a level where the binder can volatilize and kept at this until all the binder has been removed. The temperature can then be safely increased to the sintering temperature. However, if the temperature is increased before the binder has completely volatalized, the remaining portion will cause a carbon residue. In some cases, this carbon residue can cause discoloration and can even result in further reactions.

If a certain component in the mixture to be sintered does not decompose early enough, the part can be damaged due to gas evolution. If a component does not decompose completely, an inhomogenous condition can result. Carbonates in general have a high decomposition temperature, but usually do not cause a problem because the sintering temperature is above 1000 °C [22].

7.9. Sintering of Calcium Phosphates

Mostly, ceramics are produced by preforming a powder slurry and liquid (water, in most cases) into a shape or a mold and increasing the temperature to a certain point where the individual particles of the powder sinter together, depending on the time/temperature cycle. Throughout the sintering process, the void volume, referred as porosity, between the particles becomes less. The porosity is expressed as a percentage of the total volume and called the microporosity if the particle size of the powder is in micrometer range. A good sintering results in a low porosity. However, several methods exist to introduce larger pores of at least 100 μm which allow tissue ingrowth.

When the slurry is made of powder and an aqueous solution of hydrogen peroxide, heating at 80 °C and higher temperatures result in the dissociation of hydrogen peroxide as a result of which oxygen bubbles escape the drying slurry and leave behind interconnection pores the size of which may exceed 100 μm, depending on the bubble size. The bubble size is determined by the rate of temperature increase ad hydrogen peroxide content in the slurry [34].

A biological microstructure can be introduced when a skeletal microstructure is embedded with slurry, treated with acid to remove the mineral and the wax negative filled with slurry. When the wax is burned off at 400 °C, a porous positive in dried slurry is obtained. After firing, a positive replica in ceramic is obtained. Instead of wax any other porous structure that can be burned off at a lower temperature than the sintering temperature can be used, such as naphthalene.

Powders of calcium phosphate can be compacted under pressure in an ordinary press and then sintered at an appropriate temperature.

7.10. Sintering of Hydroxyapatite

Among different binders organic ones, especially polyvinyl alcohol is the most commonly practiced one in recent studies. Organic binders have the advantage of complete burn-out during sintering and good control of the sintering parameters ensures total removal of the binder from the sintered body. For this purpose, the sintering atmosphere should be controlled. The easiest way of controlling is the relatively slow increase of temperature during sintering which allows the gases resulting from the burn-out of the binder to escape the porous structure of the sample to be sintered.

Jinawath *et al.* [35] has used 1.2 % polyvinyl alcohol as a binder together with $CaO\text{-}P_2O_5$ as a sintering additive in his hydroxyapatite studies. In another study, a mixture of polyvinyl acetate and polyethylene glycol has been added to the hydroxyapatite powder as a binder [36].

Several sintering additives have been tried for hydroxyapatite in previous works. Kalita *et al.* [37] has experimented with various concentrations of $CaO\text{–}P_2O_5\text{–}Na_2O$ mixtures as a sintering additive and found out that this additive improves the mechanical as well as the biocompatibility characteristics of hydroxyapatite.

Li_3PO_4 is another sintering additive used to increase the densification during sintering [38]. Further experiments incorporating Li^+ ion as the sintering additive have been conducted and given satisfactory results [26]. The latter work has also proven the positive effect of adding Mg^{2+} ions, however, with a less success compared to Li^+. Another study has trialed the incorporation of Na_3PO_4 as an additive and resulted in improved densification characteristics during sintering.

The idea of incorporating a sintering additive into the hydroxyapatite to improve densification during sintering is to form a liquid phase at the high temperatures throughout the sintering process and to initiate liquid-phase sintering in this way. The presence of a melt during the sintering process substantially increases the area of interparticle contact and, consequently, the rate of the surface and volume diffusion.

Resulting from this, an appropriate sintering additive can decrease the effective sintering temperature 50 to 100 °C from its value without any additive.

Different opinions exist about the effective sintering temperature and about the temperature range for the sintering of hydroxyapatite ceramics. The differences in the data in the literature and their interpretations arise mainly from the fact that hydroxyapatites produced by different techniques behave differently under high temperatures. According to some studies sintering begins at 850 °C whereas others state that the first traces of sintering appear first at 1000 °C. on the other hand, some authors state that at temperatures above 1200 °C decomposition of hydroxyapatite begins whereas other workers insist that up to 1300 °C hydroxyapatite remains unchanged. Recent findings show that the latter opinions in both the unset and completion of sintering are more solid, respectively. However, all the findings are supported by electron microscopy and other elemental measurement techniques and are therefore correct and consistent in their selves. The differences are mainly based on the method of production and other factors like impurities and sintering atmosphere.

Regarding the findings in the literature it would be a safe way to enhance sintering not by rising the sintering temperature but by making the sintering time longer. This will not only ease the control of the sintering process but will also avoid the possibility of decomposition in the final structure. However, the decomposition does not only depend on high sintering temperatures but also on sintering time which means that very long sintering times do have a negative effect on the composition of the product. Therefore, it is very important to control the sintering temperature parameters like temperature range, heating and cooling rates, as well as the sintering time.

Gibson *et al.* [33] has found out that for laboratory synthesized hydroxyapatite sintering begins at 900 °C and completes at 1200 °C whereas a commercial begins to sinter at 1000 °C and reaches its maximum density at 1300 °C. Both samples have attained their maximum densities after 4 hours of sintering.

Tas *et al.* [32] have come to the conclusion that samples sintered at 1200 °C for 10 hours have reached 99.2 % of their theoretical density without any sign of decomposition of the apatitic structure. Further, they have findings about the existence of pure calcium hydroxyapatite even at 1300 °C with no sign of dehydroxylation.

Ruys *et al.* [39] have systemically observed the process of sintering of hydroxyapatite at various temperatures and have concluded that below 900 °C almost no densification takes place whereas it is accelerated between 900 and 1200 °C. After 1200 °C they have noticed the closure of pores and elimination of continuous paths from the compact interior to the surface. However, the continuing dehydroxylation resulted in a rise of internal vapor pressure which certainly has exceeded the mechanical strength of the solid and finally caused blowholes.

In their solid thermogravimetric study supported by a detailed FTIR analyzes Liao *et al.* [40] have found out that hydroxyapatite begins to decompose at 1350 °C which is in close agreement with the equilibrium diagram. They further have concluded that hydroxyapatite does not dehydrate completely before decomposition

8. EXPERIMENTAL STUDY

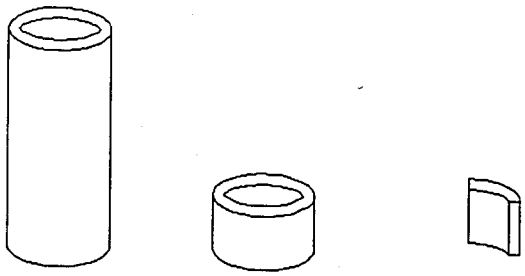
8.1. Preparation of Bones

Hydroxyapatite powder has been produced from fresh calf femur. For this purpose, fresh bone has been obtained as both ends removed. The bones are cooked in a pressurized kettle for 2 hours. The bone marrow has easily been removed because of the shrinkage as a result of the cooking. The inside and outside of the remaining bone, as a hollow cylinder, has been cleaned using a sharp knife such that all soft tissue has been removed.

The so cleaned bone has to be sectioned. The sectioning has first been tried with a hand saw but the very hard nature of the bone has made this a very tedious process. The next trial has been done with a small scale electrical band saw where the blade has been stuck in the bone. So the process could be accomplished with an industrial type electrical saw with a solid band saw. The solid band saw was obtained from the Makina Kimya Endustrisi, Turkey.

The bones have been sectioned into cylinders of 2 cm-thickness. The small cylinders have been sectioned into four equal quarters by squeezing in a clamp. The clamp jaws of the clamp have been wrapped with nylon such that no impurities from the jaw can stick on the bone parts. The bones have been sectioned in order to increase exposed surface area for further processes involving chemical reactions and calcination. For an ordinary bone sample of cylindrical shape of 3 cm. outer diameter, 2 cm. inner diameters and 8 cm. height this sectioning brings up a surface area increase of almost 60 %.

The impurities resulting from the sectioning process have been removed by using a stainless steel knife under flowing water. The resulting bone parts have further been rinsed in distilled water three times and dried at 110 °C for 2 hours.



(a) (b) (c)

Figure 8.1. Schematic showing the sectioning of a bone for further use (a) complete bone, (b) axially sectioned bone part, and (c) quarter of a an axially sectioned bone part

8.2. Determination of the Best Suitable Method for Removal of the Organic Phase from Bone to Obtain Hydroxyapatite

For the production of hydroxyapatite powder from the bone parts three different routes have been proposed which are seen in the below table. In this way, it is aimed to determine separate effects of each step, namely the degreasing effect of hexane, the deproteinizing effect of NaOH and the effect of calcination on the removal of the organic phase of the bone. Each route has been followed for three different samples and the results have been averaged in order to check consistency of the results.

Table 8.1. Three different routes to produce hydroxyapatite powder from bone

1. Route	2. Route	3. Route
Degreasing in hexane		
Deproteinization in NaOH	Deproteinization in NaOH	
Calcination	Calcination	Calcination

Hexane (C_6H_{14}) has been chosen as a degreasing agent for its known effect of removing organic fat. Also, it is easy to obtain and it is possible to recycle the hexane coming out of the process.

For the deproteinization process a chemical reagent had to be chosen which can solve the organic portion of the bone and which should not solve the hydroxyapatite.

For the deproteinization process a chemical reagent had to be chosen which can solve the organic portion of the bone and which should not solve the hydroxyapatite. Hydroxyapatite is known to be soluble in strong acids whereas it is stable in basic solutions. So sodiumhydroxide (NaOH) has been chosen for the deproteinization purposes.

Sodiumhydroxide (NaOH) has formerly been used by as a deproteinizing agent for fresh bone [41]. Gokbayrak has modified this process and has succesfully produced hydroxyapatite powder [18]. Followingly, Goren has analyzed the use of NaOH for removing the organic fragment of bone and has further determined the best suitable parameters for the NaOH-deproteinization process by varying the NaOH concentration, the reaction time and temperature [19].

Calcination is necessary to remove the organic parts remaining from the NaOH-deproteinizaiton process. Murugan *et al.* [11] have investigated the effect of different calcination temperatures on the removal of the organic phase from the bone as a stand-alone process. Gokbayrak and Goren have used calcination to complete the deproteinization after the NaOH process [18, 19].

The effect of each separate stage on the removal of the organic phase of the bone has been determined by the percent loss of weight before and after the stage as proposed by Baah *et al.* [42]. Samples have been thoroughly washed with distilled water and dried in oven at 110 °C for 2 hours before taking weight measurements.

In addition to the above described routes also deproteinization in hydrogenperoxide (H_2O_2) has been applied. However, trial runs in H_2O_2 have shown that it does not solve the organic fraction of the bone effectively but just whiteness the outer surface of the bone pieces. So, this method has not been further considered as a possible production process.

8.2.1. Route 1

Fractured bone parts were first held in excess hexane. All of the fractured parts of a single bone has been put in a 2 liter-volume glass jar filled with 1 liter hexane and shaken in a shaking water bath at room temperature for 8 hours. Following this, the parts held in hexane have further been held in the shaker in 0.5 N NaOH solutions with 1:1.2 bone-to-solution ratios at 80 °C for 36 hours. The working temperature of the water bath has been set to 80±2 °C. To determine the effect of bone-to-solution ratio a check sample has been put in 0.5 N NaOH solutions with 1:10 bone-to-solution ratio. Finally, the parts are calcined at 850 °C for 8 hours.

Hexane obtained from Merck, Germany was used throughout the experiments and NaOH solutions have been prepared using NaOH pellets from Merck, Germany. The shaking water bath, as seen in Figure 8.1., was Julabo SW22 operated at 100 rpm throughout the experiments. Calcination has been conducted in a muffle furnace, Nuve MF120, using ceramic pots as containers.

Figure 8.2. Shaking water bath used in the experiments

8.2.2. Route 2

Different from the first route, the bone parts are directly put into the NaOH solution with 1:10 bone-to-solution ratio and held at 80 °C for 24 hours. The final step was again calcination at 850 °C for 8 hours.

8.2.3. Route 3

The fractured bone parts were directly calcined at 850 °C for 8 hours without prior degreasing or deproteinization.

8.3. Determination of the Effect of Calcination Time and Temperature on the Removal of the Organic Phase from Bone

For further determining the calcination characteristics of bone a set of experiments have been designed. The bone has been sectioned into 4 equally long parts and one of the obtained subsections has been further sectioned axially into 4 parts, as described previously. Before the calcination process the bones are held in furnace at 110 °C for 2 hours to remove moisture. Following this the bone parts are weighted and put into the muffle furnace for the calcination process.

The furnace is powered up after the bone has been put into. After the furnace temperature has reached the desired value the bone is held at the set temperature for ½ hour and left to cool down to room temperature in the furnace. Following this the bone is taken out and weighted.

The same bone has been put into the furnace again and the furnace has been heated to the same temperature using the same heating rate. After another ½ hour at the set temperature the bone is weighted again. The procedure has been repeated for an additional heating of 1 and 2 hours. So, weight measurements are taken after ½, 1, 2 and 4 hours of calcination in the furnace at the desired temperature value and the set of experiments are conducted at 4 different calcination temperatures, namely 500, 700, 800

and 900 °C in order to determine the best suitable time-temperature pair for the calcination of bone which will result in the maximum loss of organic phase at the smallest temperature for the shortest amount of time.

Later this single step production process using calcination has further been modified to increase effectiveness. First, the fractured bone parts have been calcined at 850 °C for 4 hours. The parts have been ground in a mortar and pestle in order to increase the exposed surface area and have further been calcined for another 4 hours at 850 °C.

8.4. Powder Production from the Hydroxyapatite Obtained from Bone

After the organic phase has been removed the bone parts have been ground using a ceramic mortar and pestle as long as no further decrease of particles can be determined by naked eye.

To determine the flocculation characteristics of the hydroxyapatite the grinding operation has been conducted in a simple horizontal ball mill operated at 100 rpm for 8 hours with a 0.5 liter plastic container and 100 mm-diameter zirconia grinding balls. The resulting fine powder was flocculated such that it was hard to be sieved.

So, polymethylmethacrylate has been added as deflocculant in 1 % weight ratio to the hydroxyapatite powder prior to the grinding operation, which is in accordance with the literature, and the hydroxyapatite powder has further been ground in a Fritsch Planetary Ball Mill operated at half of the maximum speed. This speed has been chosen to avoid any contamination from the grinding bowl and media.

The ball mill has 500 ml. alumina containers and 10 mm-diameter yttria-stabilized-zirconia grinding balls. The container has been filled up with grinding balls, hydroxyapatite powder and distilled water, each component occupying 1/3 of the total volume of the container.

The powder has been milled for a total of 6 hours and measurements are taken at the beginning of the grinding process and at the 3rd and 6th hours in order to determine the resulting particle size reduction, distribution and the surface area.

However, literature reports that long milling times can result in dissolution of calcium phosphates [29]. To avoid this relatively shorter milling times have been chosen for the purpose of this work.

The decrease of the particle size results in the increase of the sintering reactivity of ceramic powders which means that the powder becomes denser at lower temperatures. This favors surface diffusion mechanisms instead of volume mechanisms.

Surface mechanisms lead to strengthening by producing necks between boundaries and fusion of microporosities, but do not lead to shrinkage.

8.5. Production of Ceramic Structures from the Fine Hydroxyapatite Powder

The fine ground hydroxyapatite powder has been compacted at 350 MPa using a manually operated press for 5 minutes. Gokbayrak has tried several different press pressures and has found that at pressures lower than 350 MPa the pressed parts did not show enough strength whereas parts pressed above this pressure developed cracks after sintering [18].

A steel die has been used to produce specimens of 11 mm diameter. Although the tool design allows choosing the length of the specimen as desired 3 grams of powder is used for each of the produced specimens.

The inner part of the die and its punch has been coated with vaseline prior to pressing in order to decrease the frictional forces which arise during pressing and can result in inhomogenous stress distribution in the pressed part.

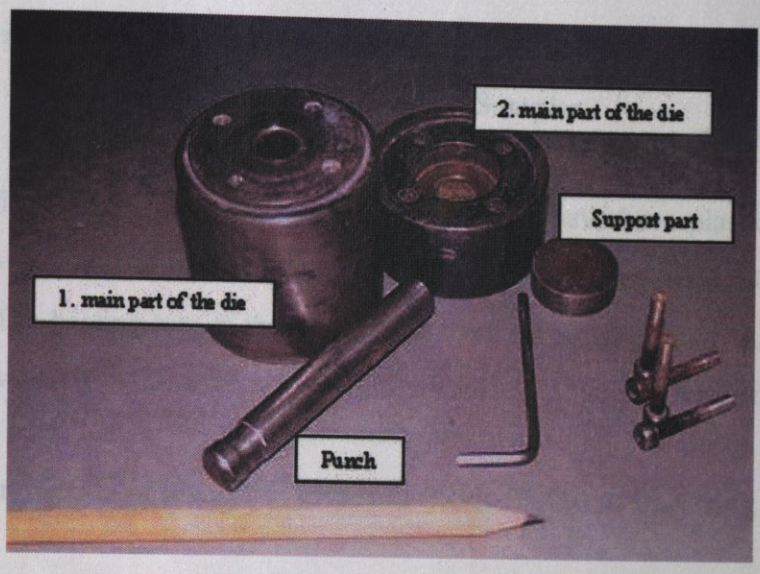


Figure 8.3. Die used to prepare the specimens [43]

Prior to pressing, stearic acid has been added to the hydroxyapatite powder to act as a lubricant during pressing and polyvinylalcohol has been added to act as a binder throughout the sintering process that will follow. Due to their organic nature both additives are expected to decompose during the sintering process.

In order to obtain proper mixing of the additives stearic acid and polyvinylalcohol have been dissolved in boiling ethanol and hydroxyapatite powder has been poured into this solution after the solving process has been completed. Other solvents like water, hexane and acetone have also been trialed but ethanol has turned out to be the only chemical among the candidates which solves polyvinylalcohol and stearic acid completely.

The ethanol has been evaporated at moderate temperatures in magnetic stirrer and the remaining powder mixture consisting of hydroxyapatite, stearic acid and polyvinylalcohol has been ground in a hand mortar to break any agglomerates remaining from the drying of the slurry.

8.6. Determination of the Effect of Sintering Time and Temperature on the Properties of the Fired Samples

As the final step the compacted ceramic structures have been placed on alumina bars and fired in a muffle furnace (Nuve MF120) at 1000, 1100 and 1200 °C for 1, 2 and 4 hours. The heating rate of the furnace has been set to 10 °C/min. After sintering the specimen was left in the furnace overnight to cool down to room temperature.

8.7. Determination of the Effect of Boron Oxide (B_2O_3) as Sintering Additive

Boron is known to play an important role in bone formation. In order to incorporate boron into the produced samples and meanwhile to investigate the effect of boron on the hydroxyapatite as a sintering additive five different batches have been prepared using polyvinylalcohol as binder, stearic acid as lubricant and boron oxide as sintering additive and all the samples have been sintered at 1200 °C for 4 hours. The existence of boron oxide is expected to initiate wet sintering in the samples and therefore enhance the state of sintering of hydroxyapatite.

Table 8.2. Batches Prepared for Sintering in Order to Determine the Effect of Boron Oxide as Sintering Additive

	Amount of Hydroxyapatite (wt. %)	Amount of Polyvinylalcohol (wt. %)	Amount of Stearic Acid (wt. %)	Amount of Boron Oxide (wt. %)
1. Batch	97	1	1	1
2. Batch	96	1	1	2
3. Batch	93	1	1	5
4. Batch	88	1	1	10
5. Batch	78	1	1	20

8.7.1. Analytical Techniques Used for Characterization of the Produced Powder and Samples

After the removal of the organic phase from the bone by the three different routes as described above and the grinding operation using a mortar and pestle infrared transmission (FT-IR) measurements were done by KBr pellet method. Also, EDAX (Philips XL ESEM-FEG&EDAX) and X-Ray (Rigaku D/Max-Ultima+/PC) analyses were conducted on the hydroxyapatite powders and ESEM (Philips XL ESEM-FEG&EDAX) micrographs have been taken.

While the grinding operation in the planetary ball mill samples were taken every 3 hours and analyzed for the particle size, particle distribution and the surface area.

X-Ray and EDAX measurements and ESEM images of the sintered bodies are obtained to determine the effects of sintering parameters such as time, temperature and sintering additive.

9. RESULTS AND DISCUSSION

9.1. Preparation of Bones

Due to the composite character of fresh bone it was a tedious work to section the bones for further processing. For this purpose hand saw and a small scale portable electrical band saw have been tried. However, effective sectioning could only be achieved with an industrial type band saw.

9.2. Determination of the Best Suitable Method for Removal of the Organic Phase from Bone to Obtain Hydroxyapatite

As mentioned before, three different routes have been applied and evaluated for the removal of the organic phase from the bone to obtain hydroxyapatite. First of all, these routes have been compared based on their effectiveness to remove the organic phase. The results of this set of experiments can be found in Table 9.1. and Figure 9.1.

The three different routes have been found to have almost the same effectiveness on the removal of the organic portion of the bone based on these values. Since calcination is the common step in all of the routes it can be concluded that calcination alone is the defining step in the amount of the organic matter removed from the bone.

Comparison of the results of the experiments conducted using three different routes shows that calcination alone is a well suitable alternative to the treatment of bone using hexane to degrease and sodium hydroxide to deproteinize the bone and calcinating afterwards. In addition to the above stated three different routes trial samples have been held in 0.5 N NaOH solutions at room temperature for 2 months. Below figures visualize the state of bone parts which are have been held in 0.5 N NaOH solutions at room temperature for 2 months. The surfaces of the parts have the signs of a vigorous reaction between the solution and the ceramic fraction of bone which points to the fact that hydroxyapatite dissolves in NaOH for a long reaction time.

Table 9.1. Comparison of the separate steps of the three different routes based on their effectiveness on the removal of the organic phase from bone

		Loss after degreas. in hexane (wt. %)	Loss after deprotein. in NaOH (wt. %)	Loss after calcin. (wt. %)	Total loss (wt. %)	Ave. total loss (wt. %)
1. Route	Sample 1	0,12	13,66	20,75	34.53	34.00
	Sample 2	0,02	16,28	17,15	33.45	
	Sample 3	0,12	9,05	24,84	34.01	
2. Route	Sample 1	-	14,84	21,05	35,90	33,95
	Sample 2	-	8,88	23,61	32,50	
	Sample 3	-	17,85	15,60	33,45	
3. Route	Sample 1	-	-	35,84	35,84	34,05
	Sample 2	-	-	32,48	32,48	
	Sample 3	-	-	33,83	33,83	

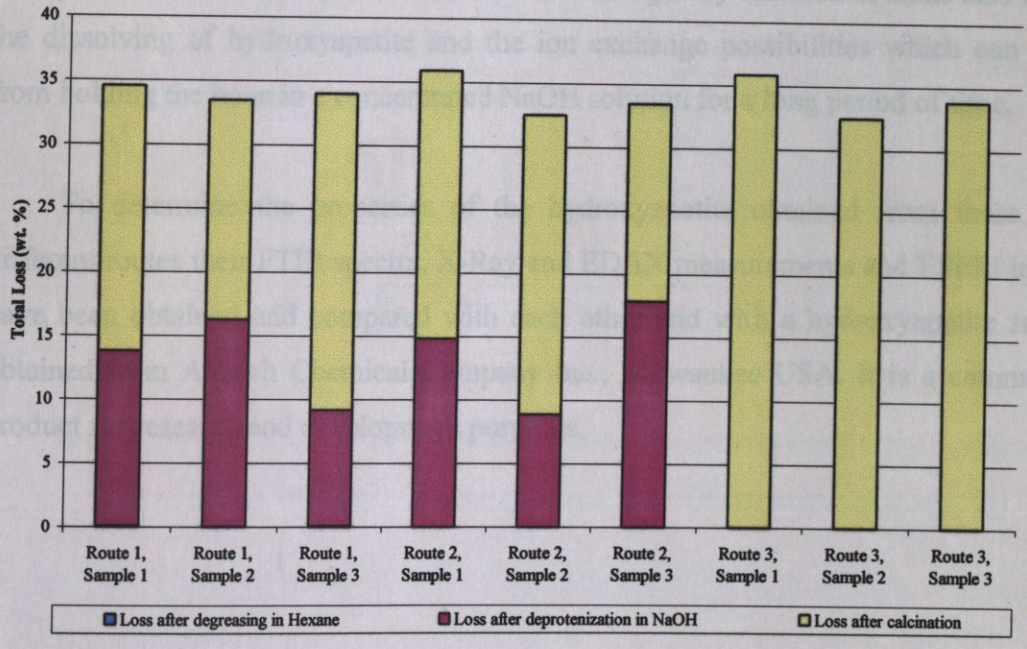


Figure 9.1. Comparison of the separate steps of the three different routes based on the wt. % of organic matter removed from bone in each step

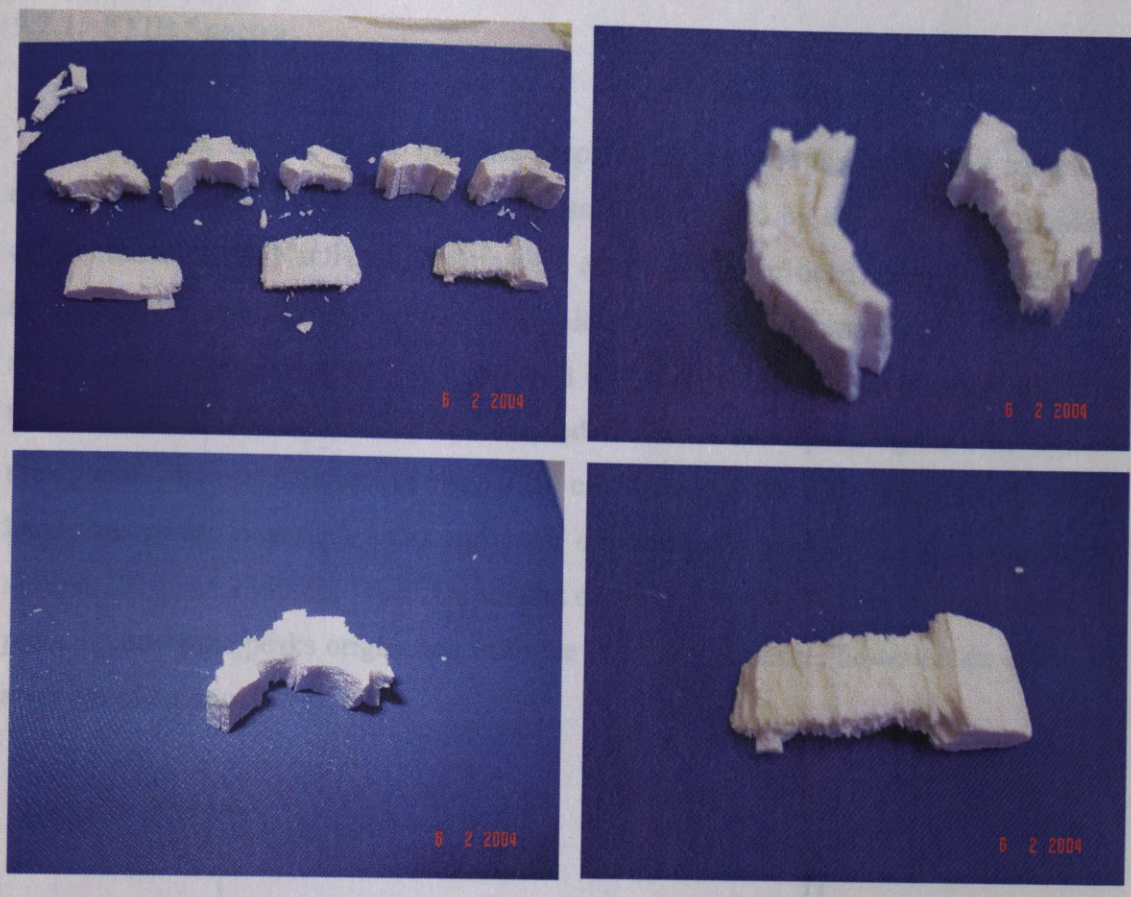


Figure 9.2. Bone parts held in 0.5 N NaOH solution for 2 months

Thus it can be stated that, in addition to its simplicity calcination alone also avoids the dissolving of hydroxyapatite and the ion exchange possibilities which can result from holding the bone in a concentrated NaOH solution for a long period of time.

To determine the properties of the hydroxyapatite obtained from these three different routes their FTIR spectra, X-Ray and EDAX measurements and ESEM images have been obtained and compared with each other and with a hydroxyapatite sample obtained from Aldrich Chemical Company Inc., Milwaukee USA. It is a commercial product for research and development purposes.

9.2.1. FTIR Spectra

The FTIR spectra of the powders prepared through the three different routes as explained in the prior section and the trial sample prepared by a long-term (2 months) deproteinization in NaOH and calcination afterwards have been compared with the spectrum of a commercial powder from Aldrich Chemical Company Inc. The FTIR spectra (% Transparency vs. wave number) of the prepared samples show absorption bands at around 470, 560, 600, 950, 1040 and 1090 cm^{-1} corresponding the PO_4^{3-} ion of the apatite. The peaks around 630 and 3560 cm^{-1} belong to the OH^- group. On the other hand, the peaks at around 1410 and 1450 cm^{-1} indicate the CO_3^{2-} and the peaks at around 2320 and 2360 cm^{-1} the CO_2 content of the powder [4, 44, 45]. The commercial powder shows the peaks originating from the PO_4^{3-} ion presence, however, do not have any sign of having CO_3^{2-} in it.

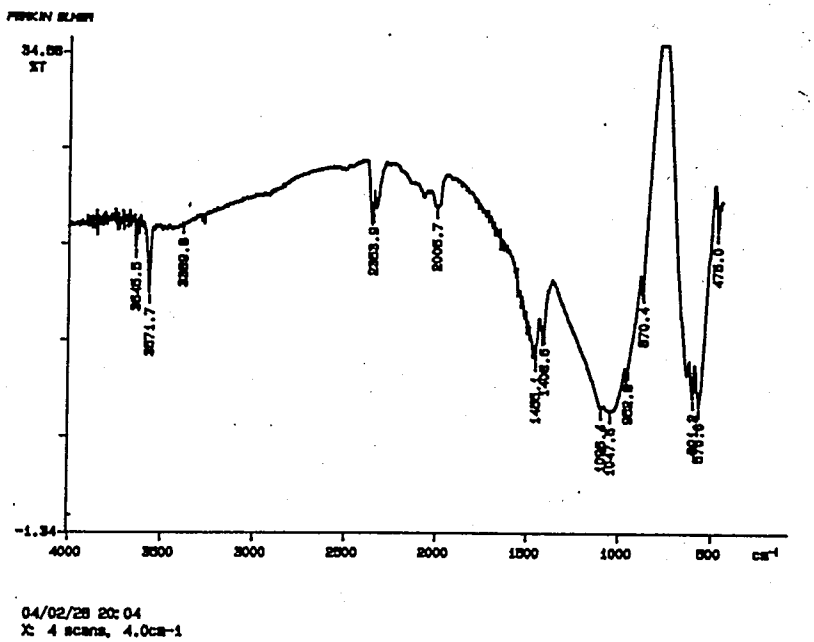


Figure 9.3. FTIR spectrum of the hydroxyapatite powder obtained using 1. Route (degreasing in hexane, deproteinization in NaOH and calcination)

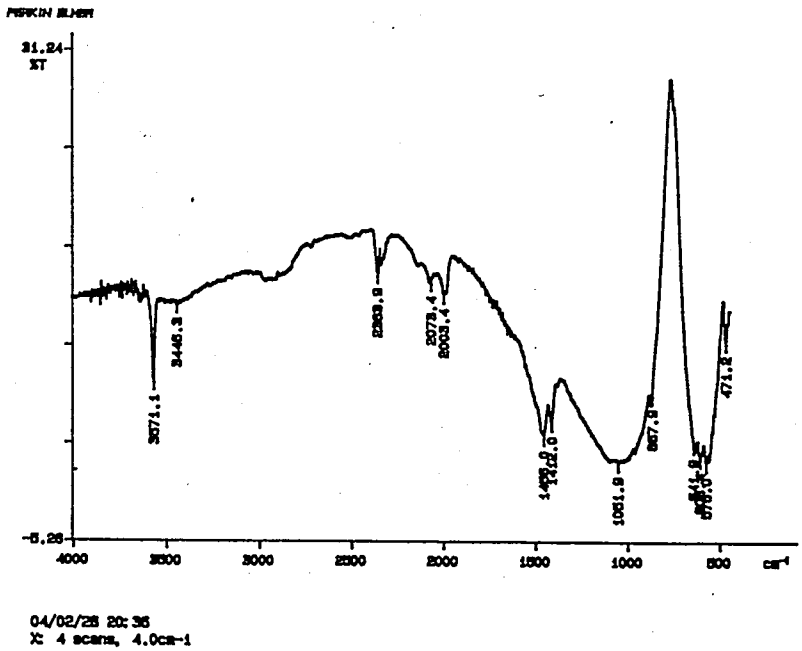


Figure 9.4. FTIR spectrum of the hydroxyapatite powder obtained using 2. Route (deproteinization in NaOH and calcination)

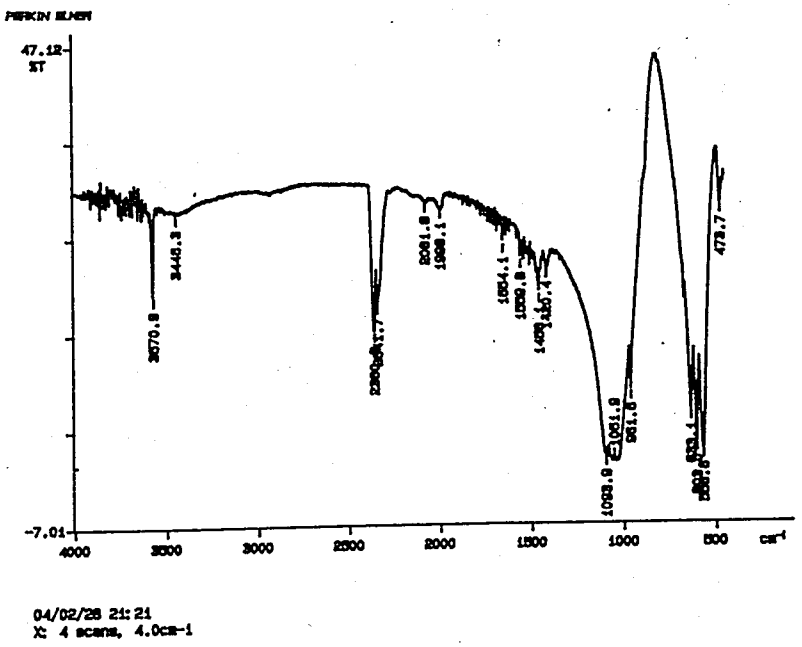


Figure 9.5. FTIR spectrum of the hydroxyapatite powder obtained using 3. Route (only calcination)

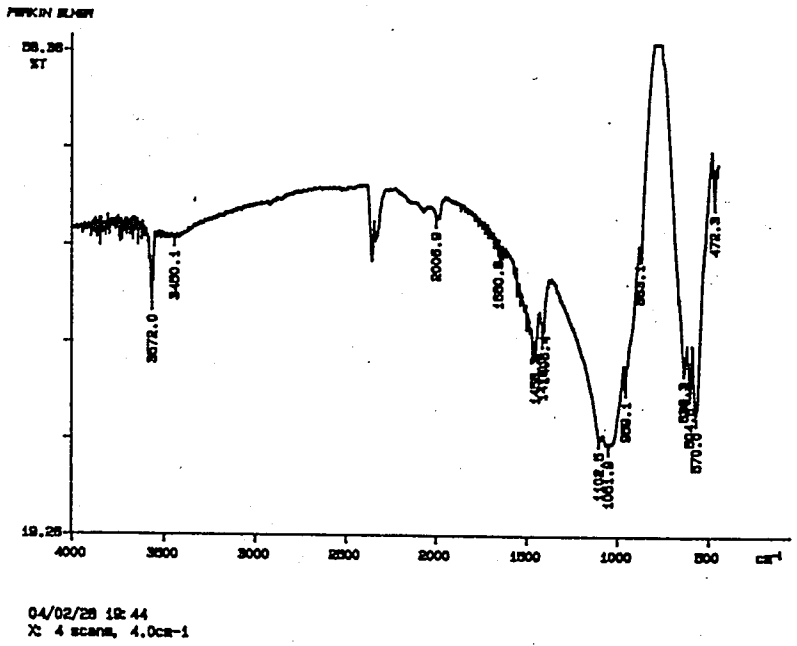


Figure 9.6. FTIR spectrum of the hydroxyapatite powder through a long-term (2 months) deproteinization in NaOH and calcination

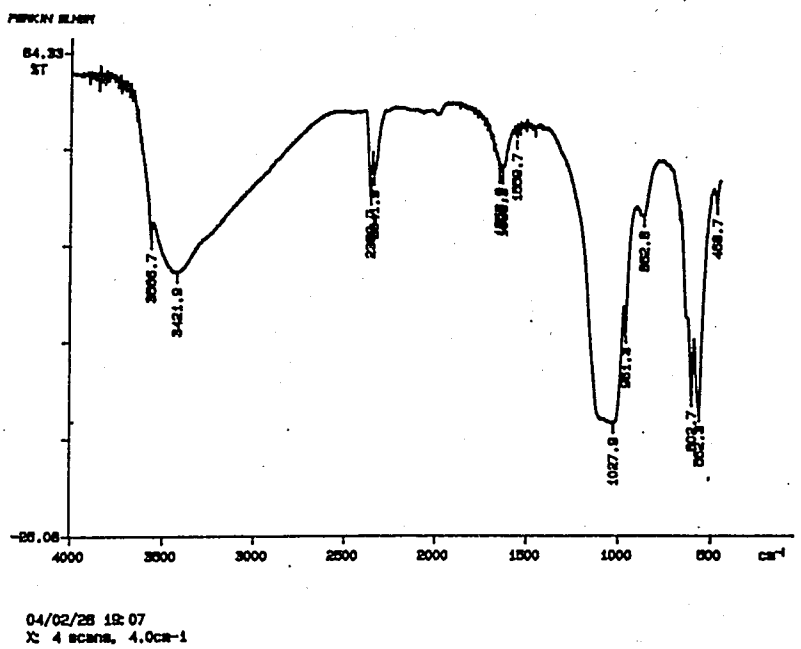


Figure 9.7. FTIR spectrum of the commercially available hydroxyapatite powder from Aldrich Chemical Company Inc.

9.2.2. X-Ray Spectra

The X-Ray spectra of the samples closely agree with the results obtained in previous research found in literature [4, 40]. The spectra of all the samples independent of the production routes show a hydroxyapatite characterized pattern, as expected. This is obvious because all of the three routes end with a calcination phase with the same temperature and time values, namely 850 °C and 8 hours, respectively.

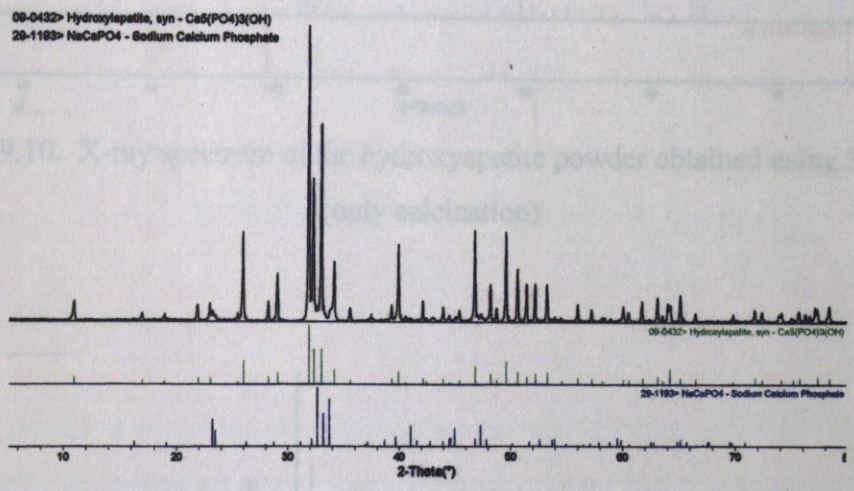


Figure 9.8. X-ray spectrum of the hydroxyapatite powder obtained using 1. Route (degreasing in hexane, deproteinization in NaOH and calcination)

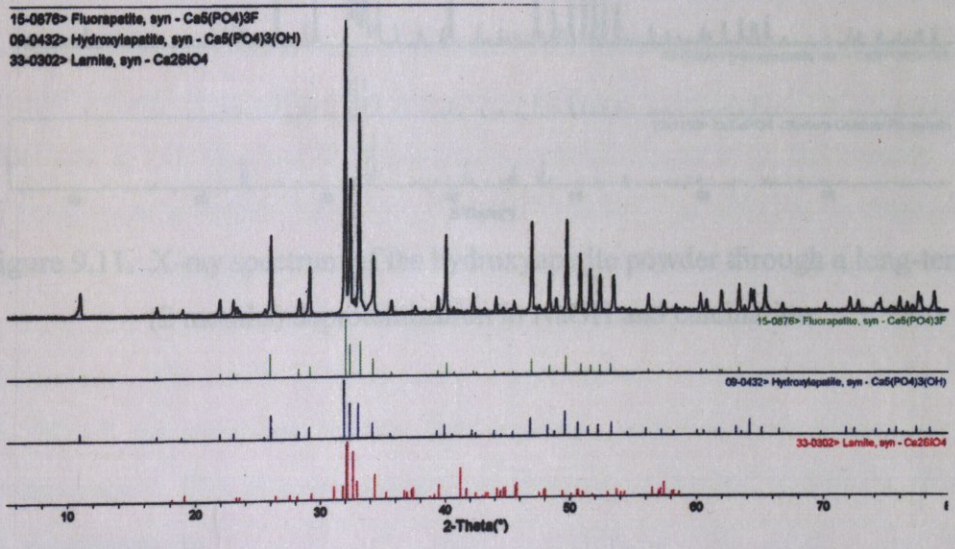


Figure 9.9. X-ray spectrum of the hydroxyapatite powder obtained using 2. Route (deproteinization in NaOH and calcination)

9.2.2. X-Ray Spectra

The X-Ray spectra of the samples closely agree with the results obtained in previous research found in literature [4, 40]. The spectra of all the samples independent of the production routes show a hydroxyapatite characterized pattern, as expected. This is obvious because all of the three routes end with a calcination phase with the same temperature and time values, namely 850 °C and 8 hours, respectively.

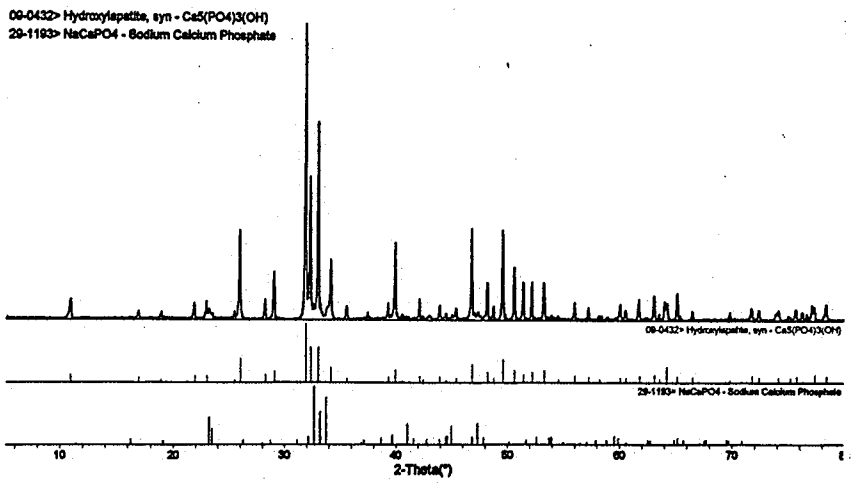


Figure 9.8. X-ray spectrum of the hydroxyapatite powder obtained using 1. Route (degreasing in hexane, deproteinization in NaOH and calcination)

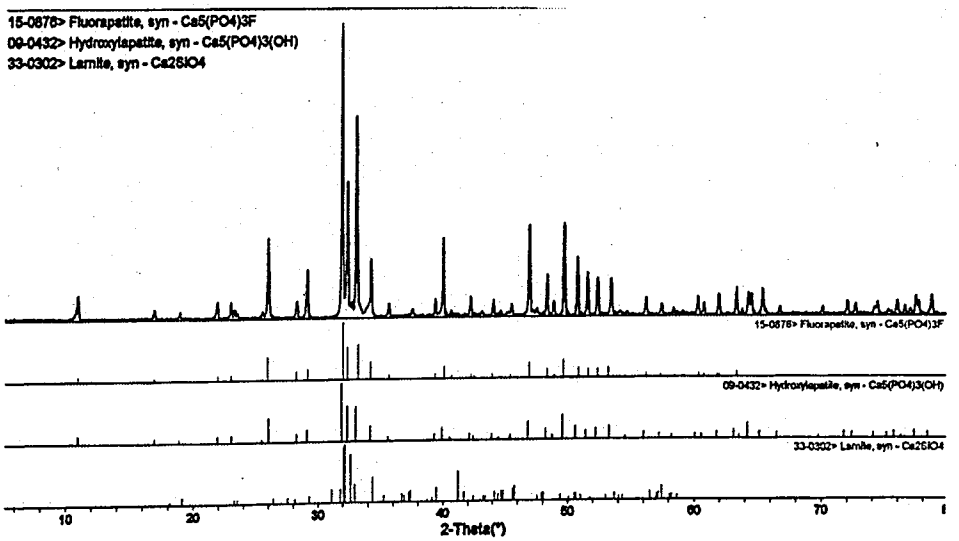


Figure 9.9. X-ray spectrum of the hydroxyapatite powder obtained using 2. Route (deproteinization in NaOH and calcination)

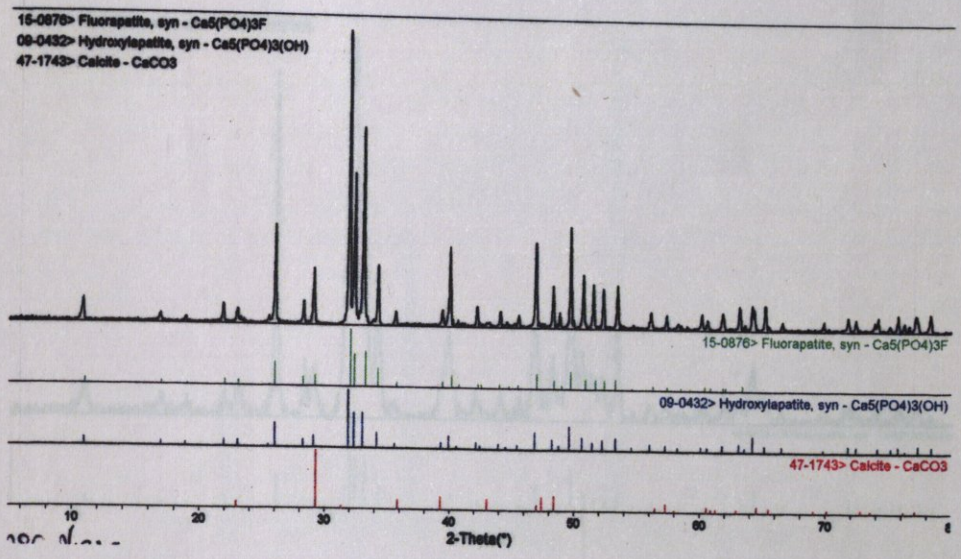


Figure 9.10. X-ray spectrum of the hydroxyapatite powder obtained using 3. Route (only calcination)

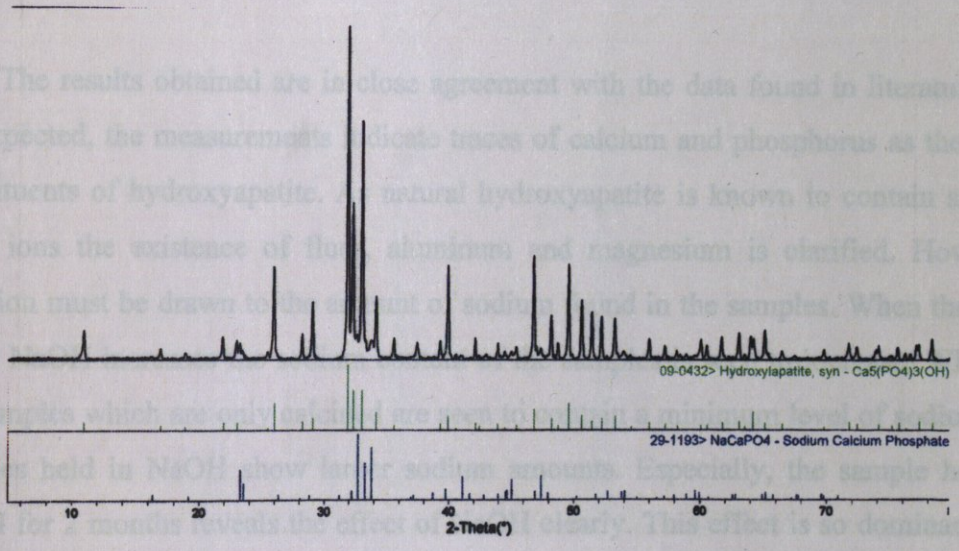


Figure 9.11. X-ray spectrum of the hydroxyapatite powder through a long-term (2 months) deproteinization in NaOH and calcination

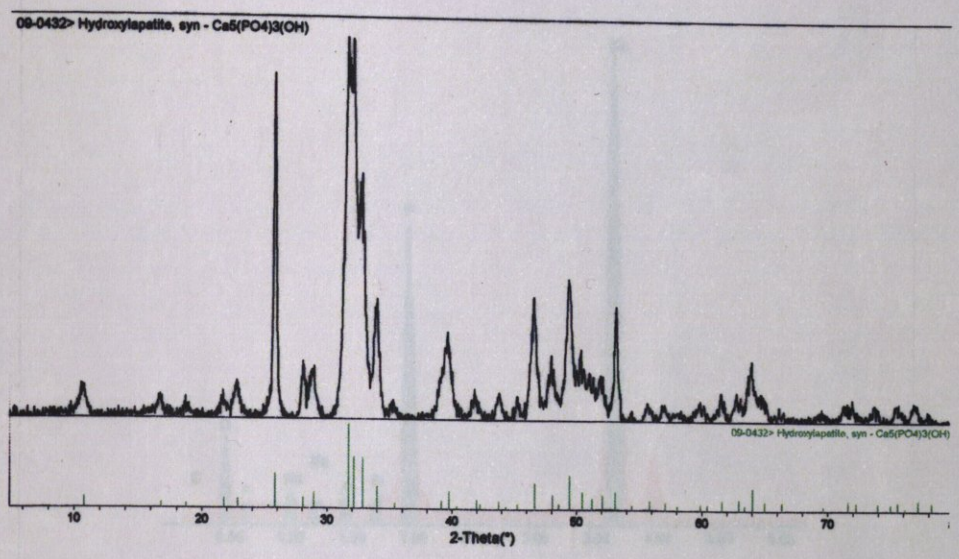


Figure 9.12. X-ray spectrum of the commercially available hydroxyapatite powder from Aldrich Chemical Company Inc.

9.2.3. EDAX Spectra

The results obtained are in close agreement with the data found in literature [4]. As expected, the measurements indicate traces of calcium and phosphorus as the main constituents of hydroxyapatite. As natural hydroxyapatite is known to contain several other ions the existence of fluor, aluminum and magnesium is clarified. However, attention must be drawn to the amount of sodium found in the samples. When the time in the NaOH increases the sodium content of the samples is seen to increase. Whereas the samples which are only calcined are seen to contain a minimum level of sodium the samples held in NaOH show larger sodium amounts. Especially, the sample held in NaOH for 2 months reveals the effect of NaOH clearly. This effect is so dominant that existence of a forming phase is observed in the ESEM of the samples held in NaOH for a long time. The sample of Route 1 and the sample held in NaOH for 2 months justify this observation. The newly forming phase is seen to have a lighter color in the ESEM images. EDAX measurements in these light regions reveal that these regions are richer in sodium content. This phenomenon can be observed in the last two of the following EDAX measurements.

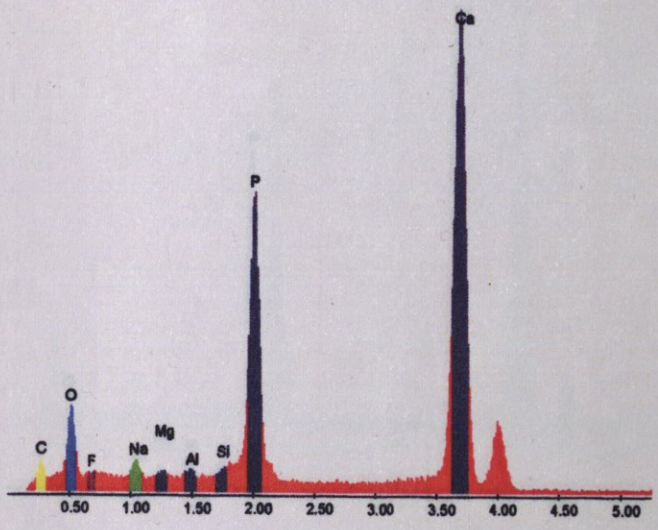


Figure 9.13. EDAX spectrum of the hydroxyapatite powder obtained using 1. Route (degreasing in hexane, deproteinization in NaOH and calcination)

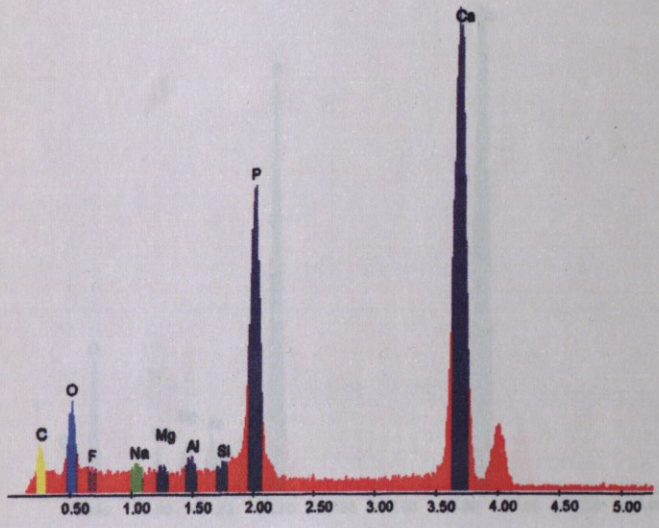


Figure 9.14. EDAX spectrum of the hydroxyapatite powder obtained using 2. Route (deproteinization in NaOH and calcination)

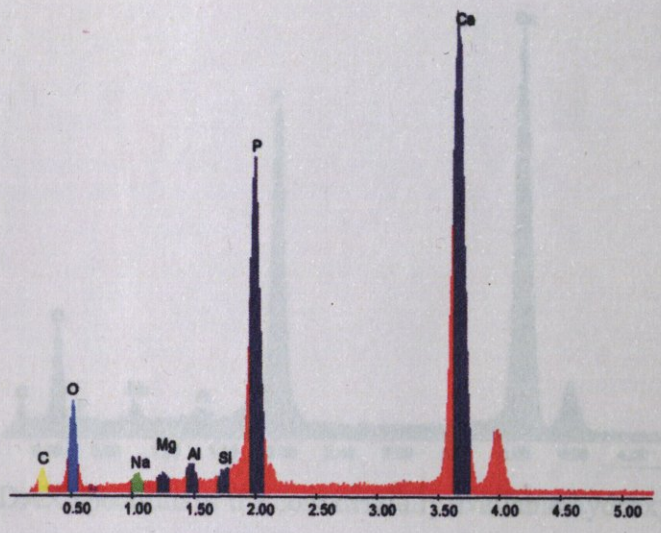


Figure 9.15. EDAX spectrum of the hydroxyapatite powder obtained using 3. Route (only calcination)

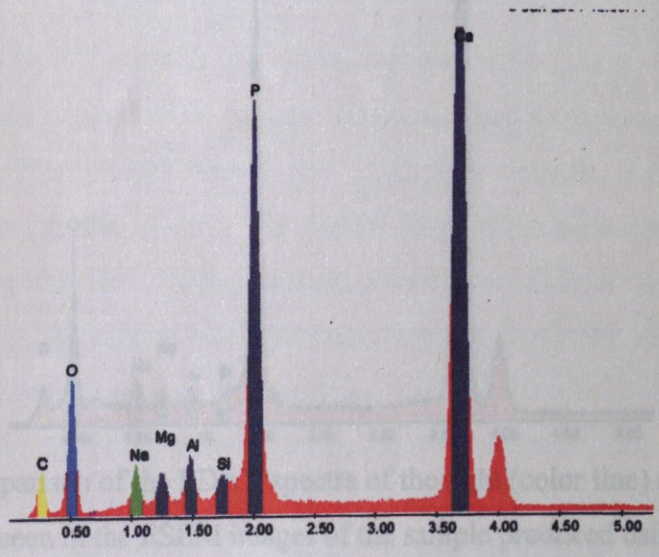


Figure 9.16. EDAX spectrum of the hydroxyapatite powder through a long-term (2 months) deproteinization in NaOH and calcination

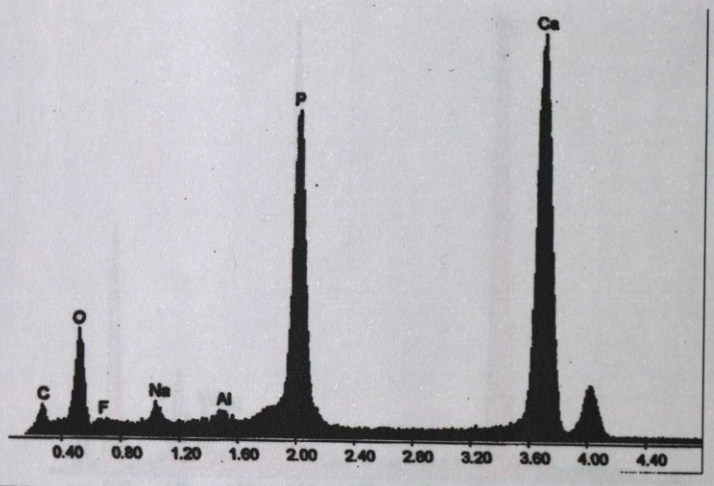


Figure 9.17. EDAX spectrum of the commercially available hydroxyapatite powder from Aldrich Chemical Company Inc. [19]

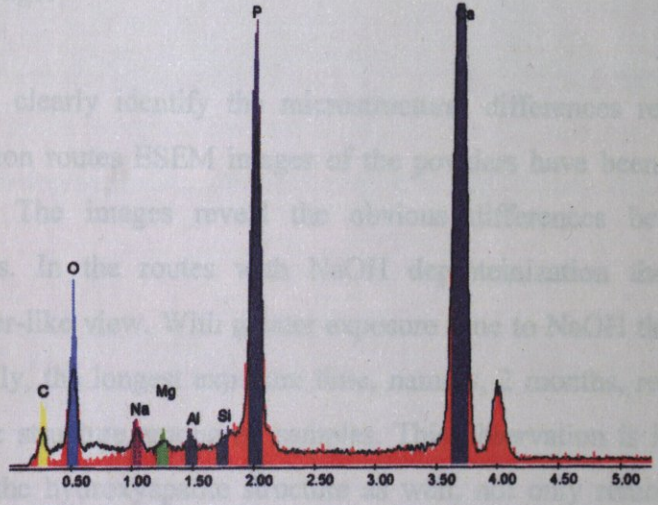


Figure 9.18. Comparison of the EDAX spectra of the light (color line) and dark regions (ghost line) seen in the ESEM images of the sample produced using Route 1

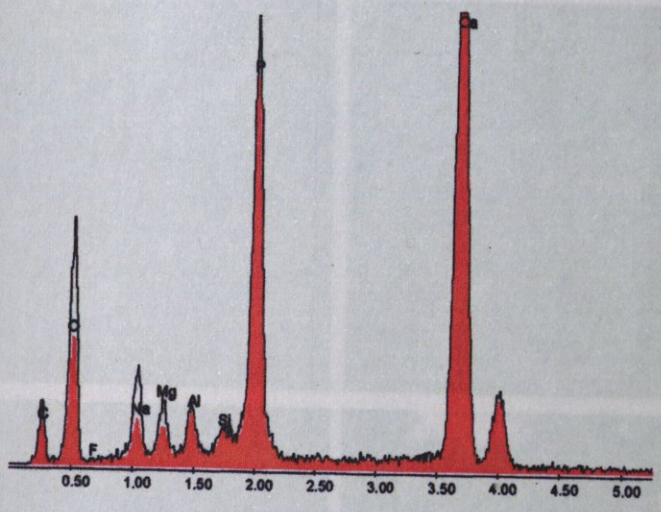


Figure 9.19. Comparison of the EDAX spectra of the light (ghost line) and dark regions (color line) seen in the ESEM images of the sample held in NaOH for 2 months

9.2.4. ESEM Images

In order to clearly identify the microstructural differences resulting from the different production routes ESEM images of the powders have been taken at various magnifications. The images reveal the obvious differences between the three production routes. In the routes with NaOH deproteinization the powder has a characteristic layer-like view. With greater exposure time to NaOH this becomes more obvious and finally, the longest exposure time, namely, 2 months, results in the most obvious layer-like structure among all samples. This observation is interpreted as the NaOH affecting the hydroxyapatite structure as well, not only removing the organic phase of the bone. As stated before, the EDAX measurements have determined regions of increased Na concentration in the samples treated with NaOH. These regions are clearly identified as having a brighter color in the ESEM images. Conclusively, NaOH has a chemical effect on the hydroxyapatite part of the bone changing its microstructure as well depositing at various regions, additionally.

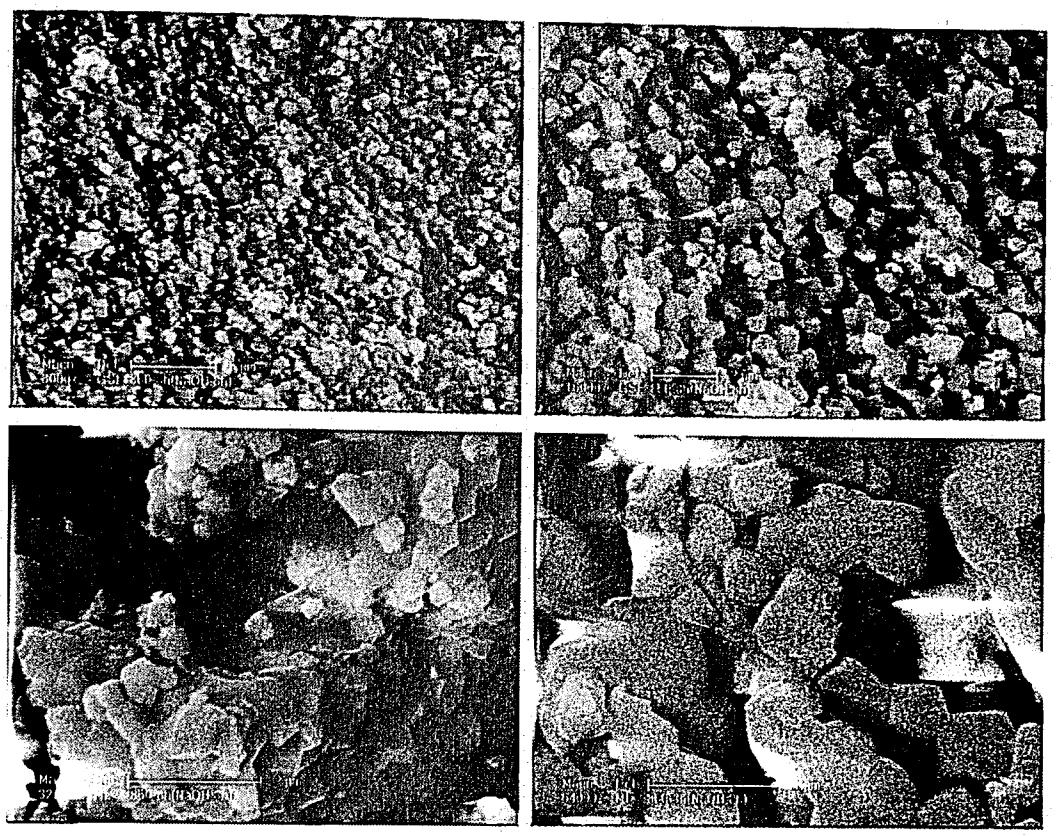


Figure 9.20. ESEM image of the hydroxyapatite powder obtained using 1. Route (degreasing in hexane, deproteinization in NaOH and calcination)

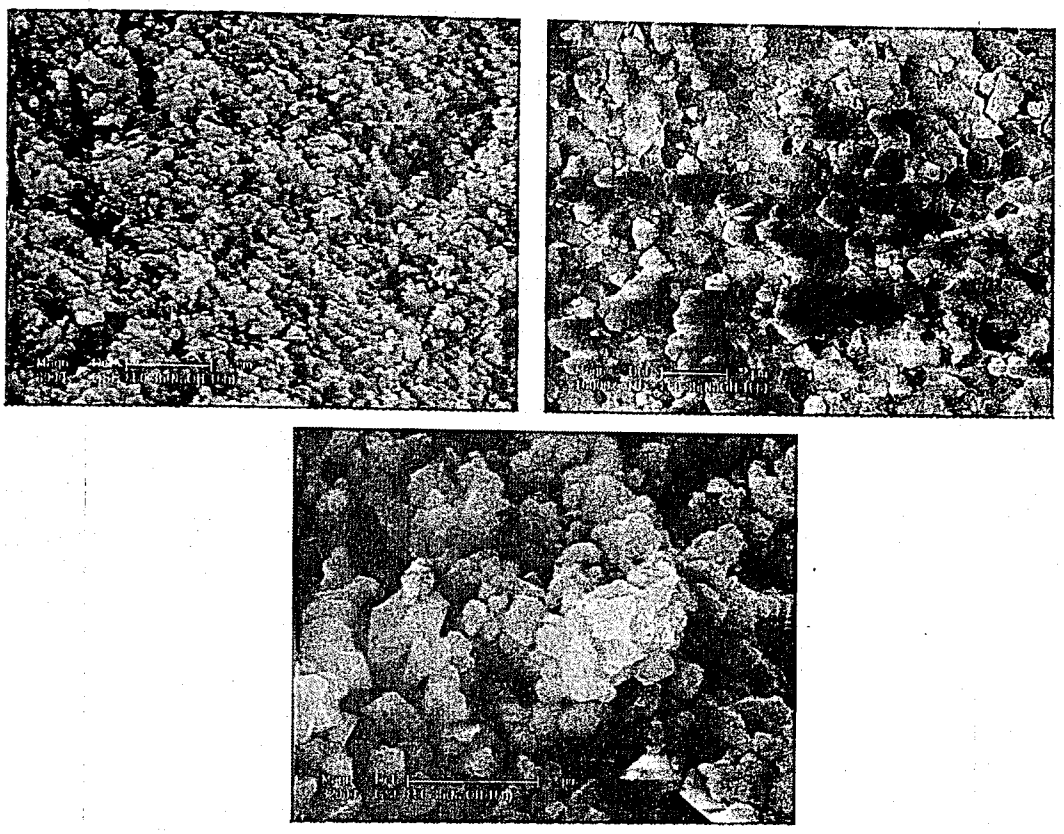


Figure 9.21. ESEM image of the hydroxyapatite powder obtained using 2. Route (deproteinization in NaOH and calcination)

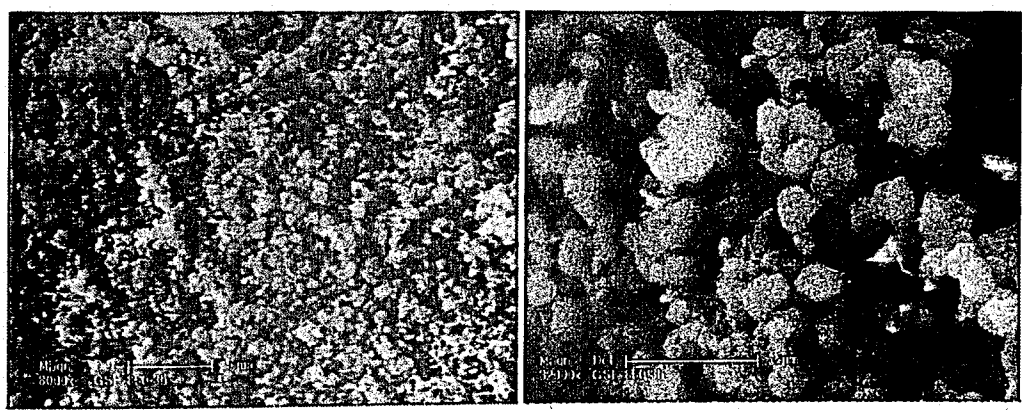


Figure 9.22. ESEM image of the hydroxyapatite powder obtained using 3. Route (only calcination)

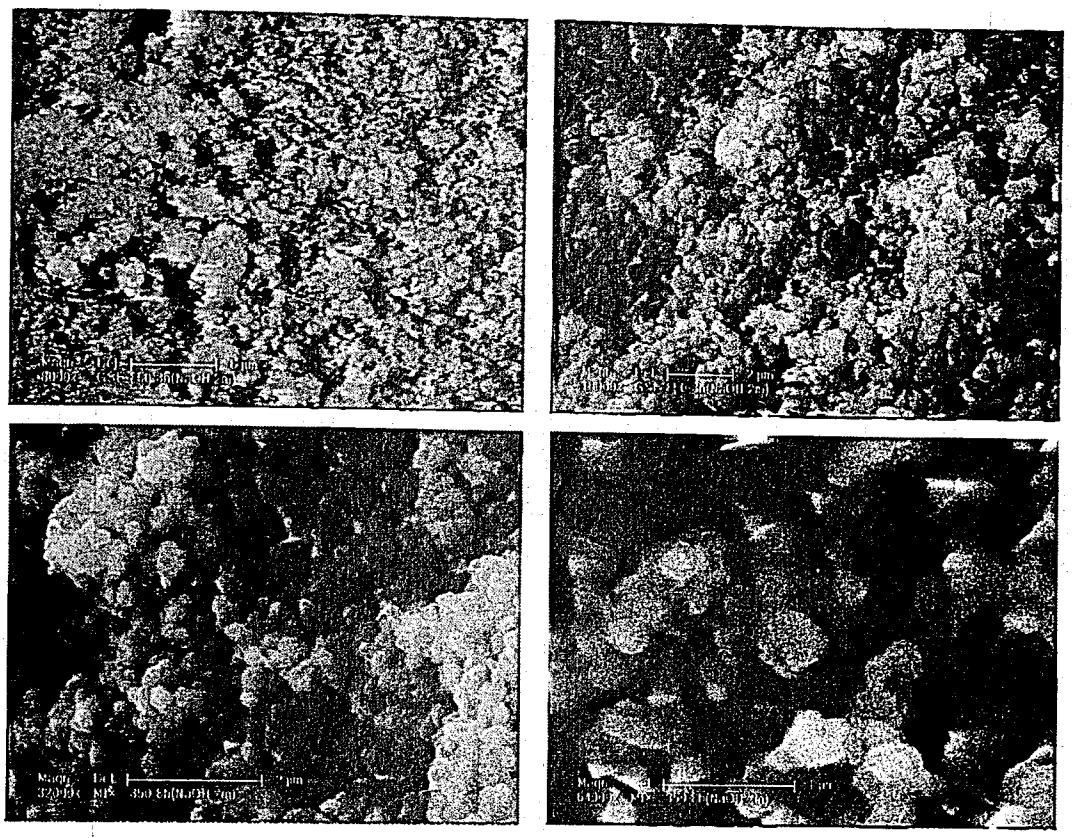


Figure 9.23. ESEM image of the hydroxyapatite powder through a long-term (2 months) deproteinization in NaOH and calcination

Figure 9.24. ESEM image of the commercially available hydroxyapatite powder from Aldrich Chemical Company Inc. [19]

9.3. Determination of the Effect of Calcination Time and Temperature on the Removal of the Organic Phase from Bone

Comparison of the results of the experiments conducted using three different routes as stated before shows that calcination alone is a well suitable alternative to the treatment of bone using hexane to degrease and sodium hydroxide to deproteinize the bone and calcinating afterwards. A simple-step calcination procedure not only eases the production of hydroxyapatite by shortening the time required to obtain the powder by cancelling any degreasing and deproteinizaiton steps but it also avoids the chemical effects NaOH and the deposition of Na in the produced powder. So, a single-step calcination has been found out a well suitable way to produce hydroxyapatite from raw bone and needs further insight.

In order to determine the best suitable set of temperature-time values for the calcination process a bone, which is cooked in a pressure pot for 1 hour and cleaned from its soft tissues using a knife, has been used. The so obtained bone is cleaned using distilled water thoroughly.

The bone has been sectioned into 4 equally long parts. One of the obtained subsections has been further sectioned axially into 4 parts. Before the calcination process the bones are held in furnace at 110 °C for 2 hours to remove moisture. Following this the bone parts are weighted and put into the muffle furnace for the calcination process.

The furnace is powered up after the bone has been put into. After the furnace temperature has reached the desired value the bone is held at the set temperature for ½ hour and left to cool down to room temperature in the furnace. Following this the bone is taken out and weighted.

The same bone has been put into the furnace again and the furnace has been heated to the same temperature using the same heating rate. After another ½ hour at the set temperature the bone is weighted again. The procedure has been repeated for an

additional heating of 1 and 2 hours. So, weight measurements are taken after ½, 1, 2 and 4 hours of calcination in the furnace at the desired temperature value.

The set of experiments are conducted at 4 different calcination temperatures, namely 500, 700, 800 and 900 °C. The calcined samples have been ground by hand using a mortar and pestle before taking further measurements and ESEM images.

Table 9.2. Percent loss of mass resulting from the experiment set to obtain the best-suitable calcination temperature and time

	% wt. loss after ½ hour	% wt. loss after 1 hour	% wt. loss after 2 hours	% wt. loss after 4 hours
Calcination at 500 °C	28,34	29,07	29,62	29,62
Calcination at 700 °C	34,66	34,82	34,97	34,97
Calcination at 800 °C	35,04	35,19	35,34	35,34
Calcination at 900 °C	35,03	35,19	35,34	35,34

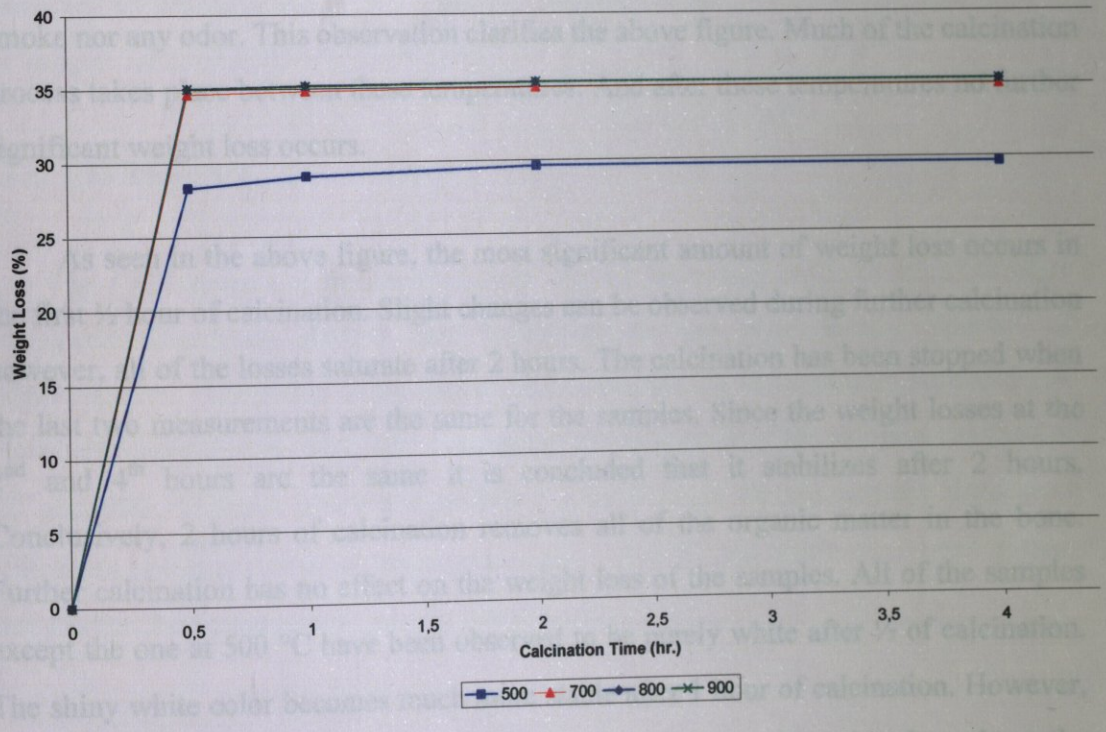


Figure 9.25. Per cent wt. loss vs. calcination time at different calcination temperatures

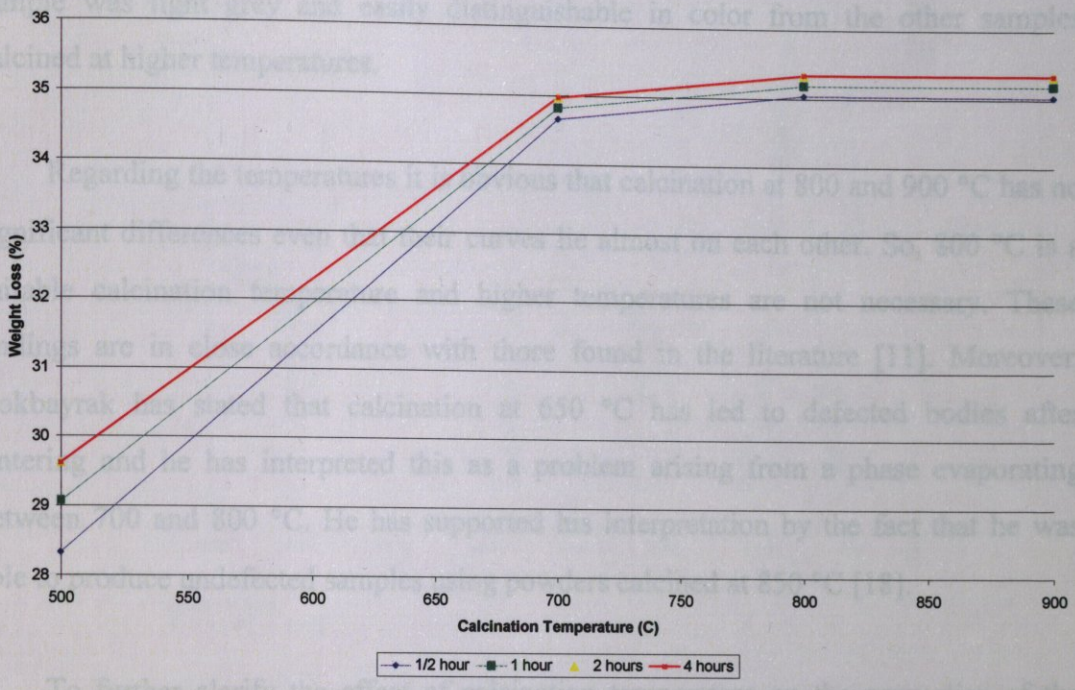


Figure 9.26. Per cent wt. loss vs. calcination temperature at different calcination times

During calcination a grey smoke and unpleasant odor starts to form beginning at 300 °C and these continue until 400 °C vigorously. After 450 °C there is neither any smoke nor any odor. This observation clarifies the above figure. Much of the calcination process takes place between these temperatures. And after these temperatures no further significant weight loss occurs.

As seen in the above figure, the most significant amount of weight loss occurs in the first ½ hour of calcination. Slight changes can be observed during further calcination however, all of the losses saturate after 2 hours. The calcination has been stopped when the last two measurements are the same for the samples. Since the weight losses at the 2^{nd} and 4^{th} hours are the same it is concluded that it stabilizes after 2 hours. Conclusively, 2 hours of calcination removes all of the organic matter in the bone. Further calcination has no effect on the weight loss of the samples. All of the samples except the one at 500 °C have been observed to be purely white after ½ of calcination. The shiny white color becomes much more stable after 1 hour of calcination. However, the sample calcined at 500 °C has maintained a grayish white color throughout the process. Although slightly whitening through time even after 4 hours of calcination the

sample was light grey and easily distinguishable in color from the other samples calcined at higher temperatures.

Regarding the temperatures it is obvious that calcination at 800 and 900 °C has no significant differences even that their curves lie almost on each other. So, 800 °C is a suitable calcination temperature and higher temperatures are not necessary. These findings are in close accordance with those found in the literature [11]. Moreover, Gokbayrak has stated that calcination at 650 °C has led to defected bodies after sintering and he has interpreted this as a problem arising from a phase evaporating between 700 and 800 °C. He has supported his interpretation by the fact that he was able to produce undefected samples using powders calcined at 850 °C [18].

To further clarify the effect of calcination temperature on the properties of the produced samples their FTIR spectra, X-Ray and EDAX measurements and ESEM images have been compared with each other and with the commercial hydroxyapatite from Aldrich Chemical Company Inc. The effect of calcination temperature has been visualized by the comparison of the samples calcined at 500, 700, 800 and 900 °C with the sample calcined at 850 °C for 8 hours.

9.3.1. FTIR Spectra

The FTIR spectra of the samples show that by increasing calcination temperature the spectra becomes sharper and resembles to the characteristic spectra of hydroxyapatite. This is due to the fact at higher calcination temperatures no additional organic compounds can exist. The comparison of the spectra of the samples calcined at 800 and 900 °C for 4 hours and at 850 °C for 8 hours do not contain significant differences pointing that at all temperatures above 800 °C and calcination times greater than 4 hours the powders have similar constituents.

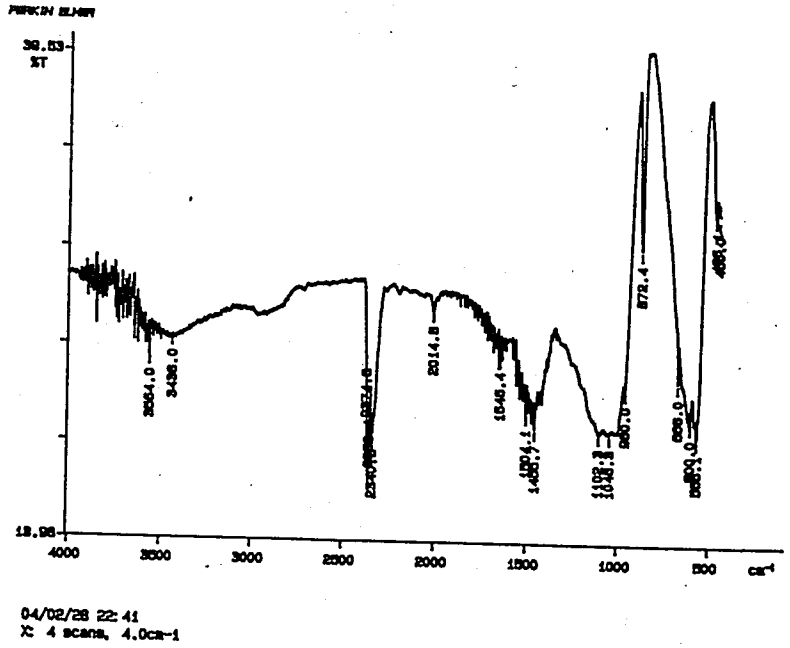


Figure 9.27. FTIR spectrum of the sample calcined at 500°C for 4 hours

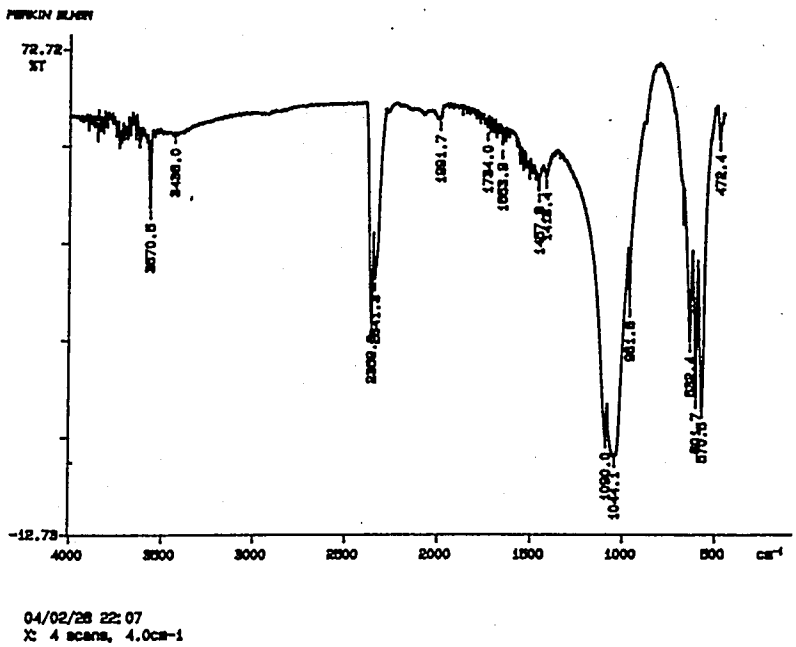


Figure 9.28. FTIR spectrum of the sample calcined at 700°C for 4 hours

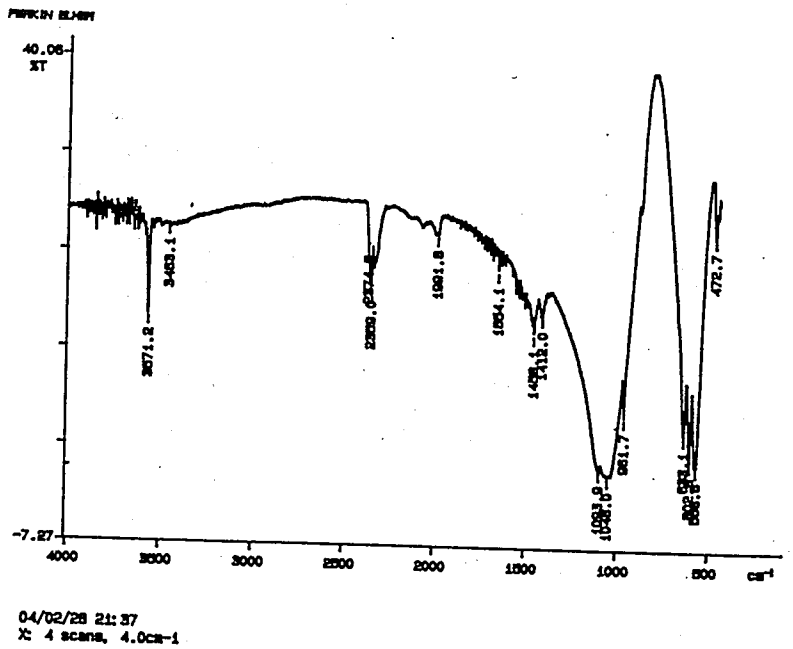


Figure 9.29. FTIR spectrum of the sample calcined at 800°C for 4 hours

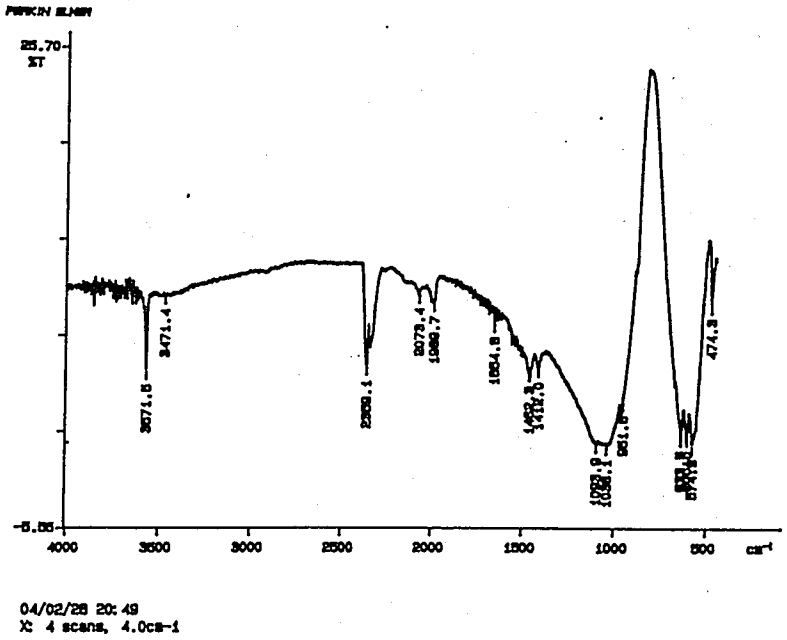


Figure 9.30. FTIR spectrum of the sample calcined at 900°C for 4 hours

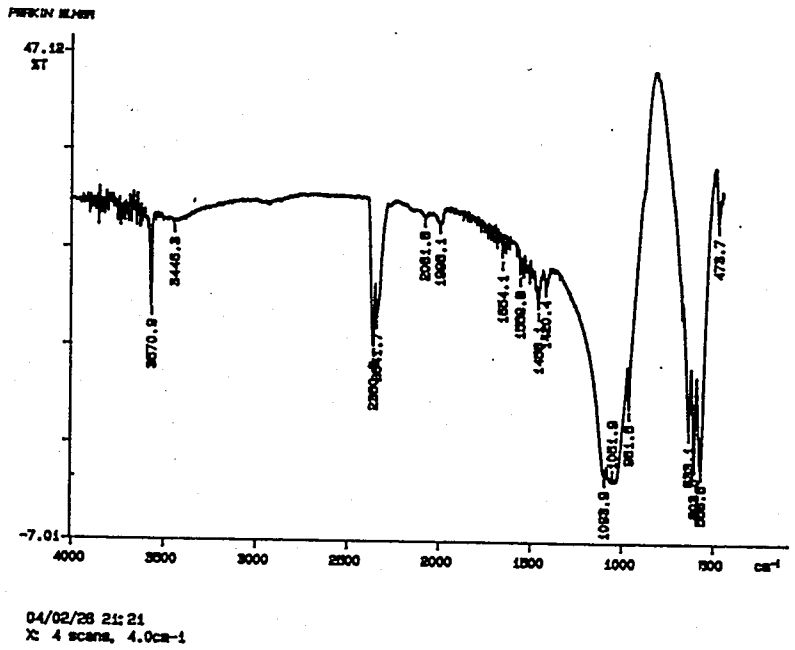


Figure 9.31. FTIR spectrum of the sample calcined at 850°C for 8 hours

9.3.2. X-Ray Spectra

The X-ray spectra of the samples reveal that there is a major difference in the crystallographic structure of the sample calcined at 500 °C and the other samples calcined at 700 °C and above. The samples calcined at 700, 800 and 900 for 4 hours °C show no noises in their spectra pointing that they have a solid crystal structure. This is supported by fact that at calcination temperatures of 700 and above decomposition of all the organic matter in bone goes to completion such that the samples calcined at 700 °C and above only contain hydroxyapatite. There is obviously no difference between the samples calcined at 800 and 900 °C for 4 hours and the sample calcined at 850 °C for 8 hours regarding their X-ray spectra.

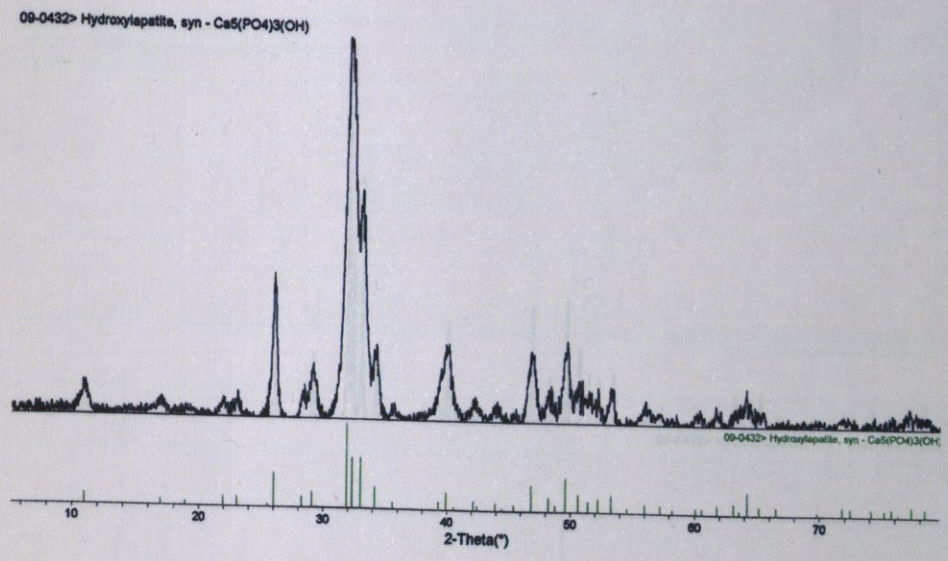


Figure 9.32. X-ray spectrum of the sample calcined at 500°C for 4 hours

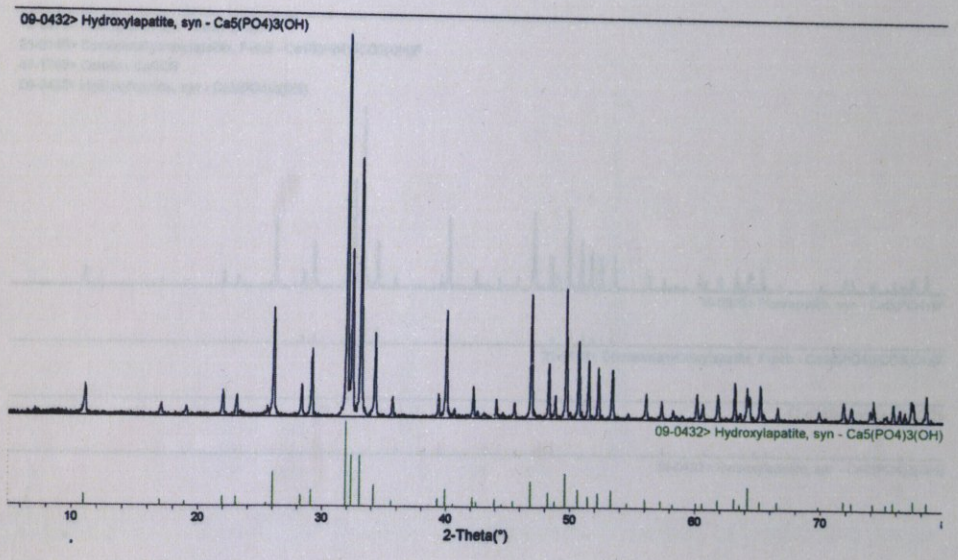


Figure 9.33. X-ray spectrum of the sample calcined at 700°C for 4 hours

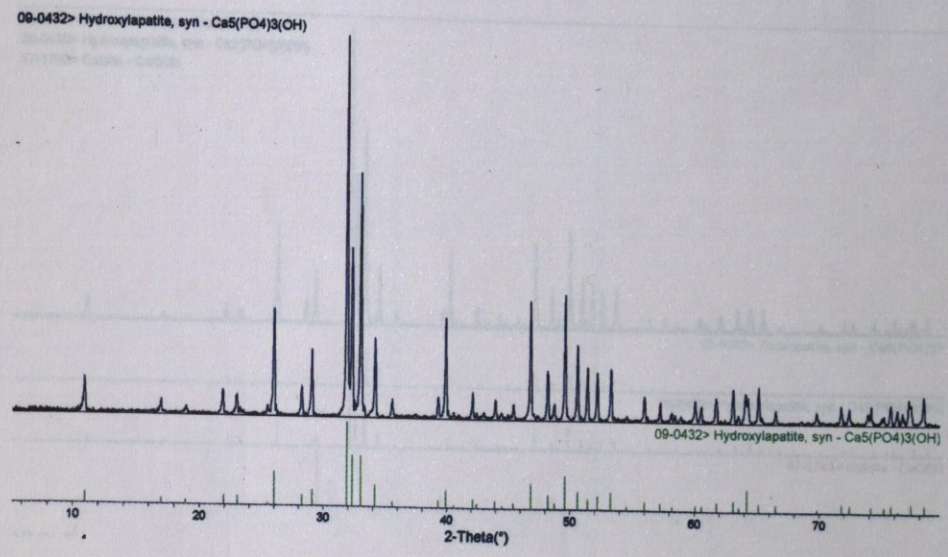


Figure 9.34. X-ray spectrum of the sample calcined at 800°C for 4 hours

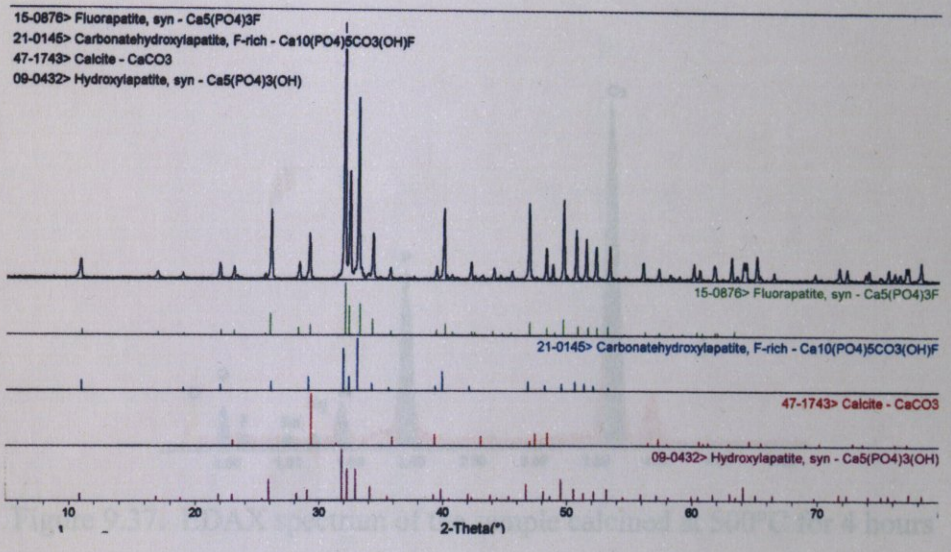


Figure 9.35. X-ray spectrum of the sample calcined at 900°C for 4 hours

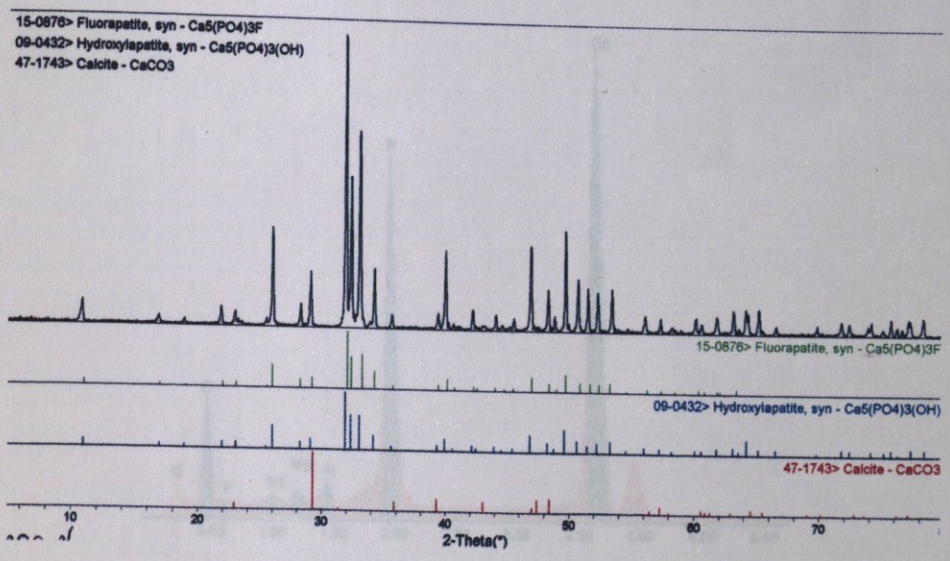


Figure 9.36. X-ray spectrum of the sample calcined at 850°C for 8 hours

9.3.3. EDAX Spectra

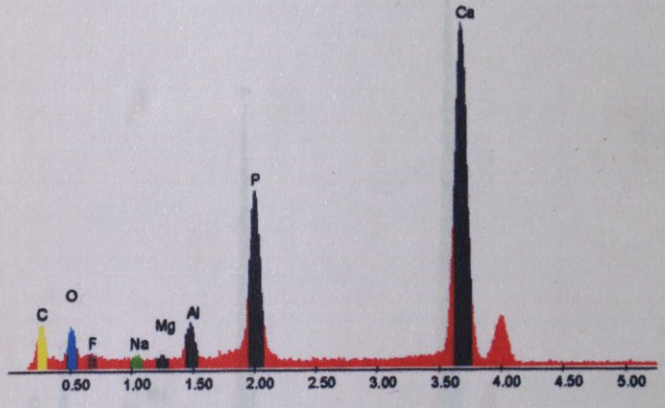


Figure 9.37. EDAX spectrum of the sample calcined at 500°C for 4 hours

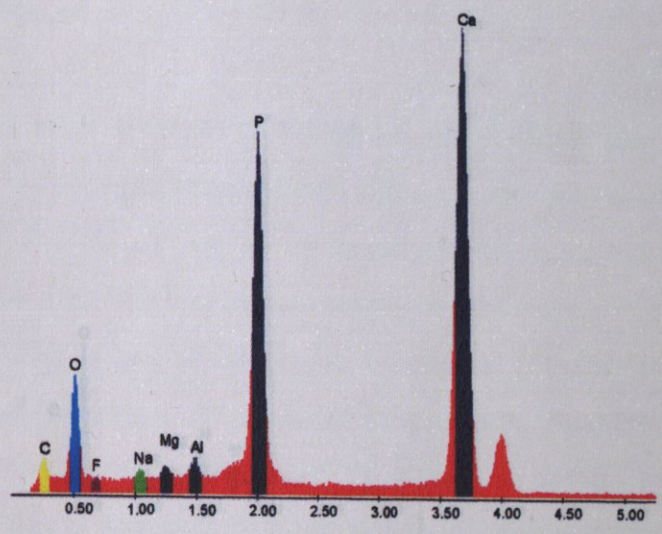


Figure 9.38. EDAX spectrum of the sample calcined at 700°C for 4 hours

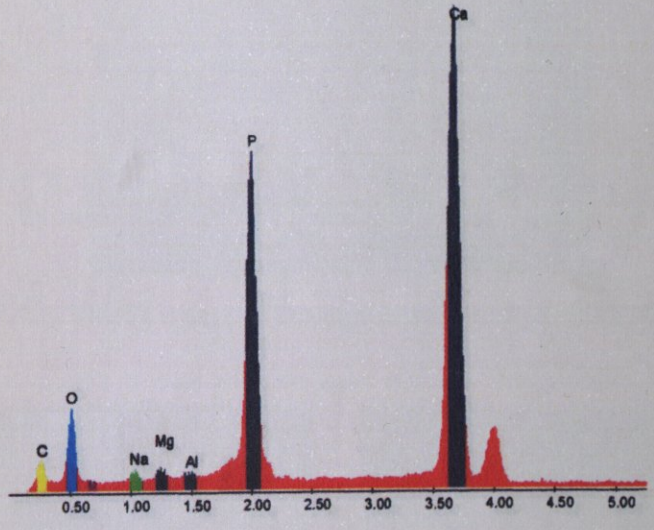


Figure 9.39. EDAX spectrum of the sample calcined at 800°C for 4 hours

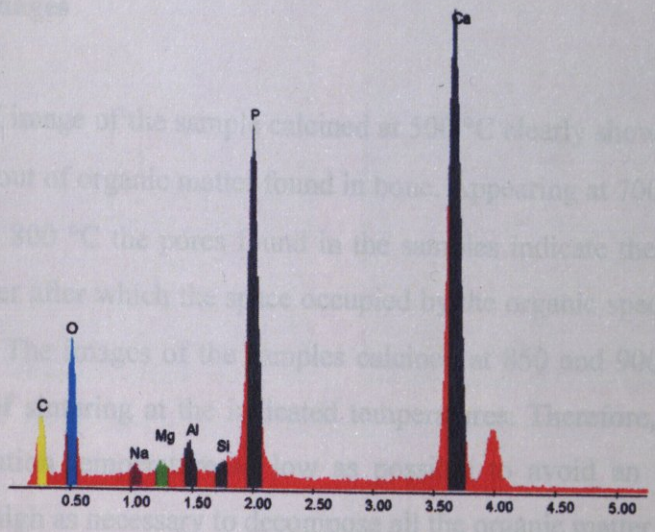


Figure 9.40. EDAX spectrum of the sample calcined at 900°C for 4 hours

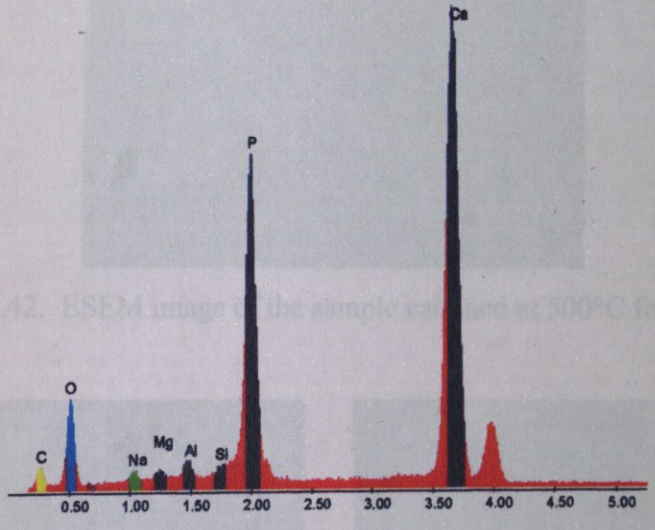


Figure 9.41. EDAX spectrum of the sample calcined at 850°C for 8 hours

9.3.4. ESEM Images

The ESEM image of the sample calcined at 500 °C clearly shows the uncompleted state of burning out of organic matter found in bone. Appearing at 700 °C and becoming more obvious at 800 °C the pores found in the samples indicate the decomposition of the organic matter after which the space occupied by the organic species is left as pores in the structure. The images of the samples calcined at 850 and 900 °C gives an idea about the start of sintering at the indicated temperatures. Therefore, it is necessary to keep the calcination temperature as low as possible to avoid an undesired start of sintering but as high as necessary to decompose all the organic matter present.

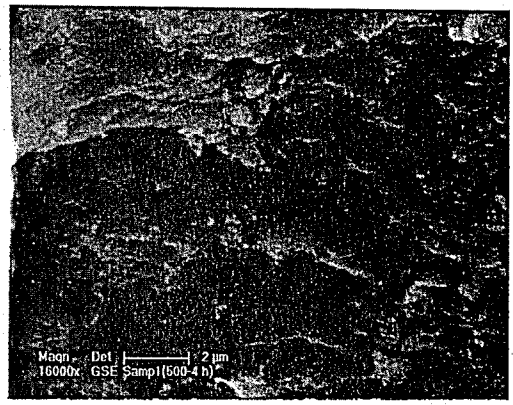
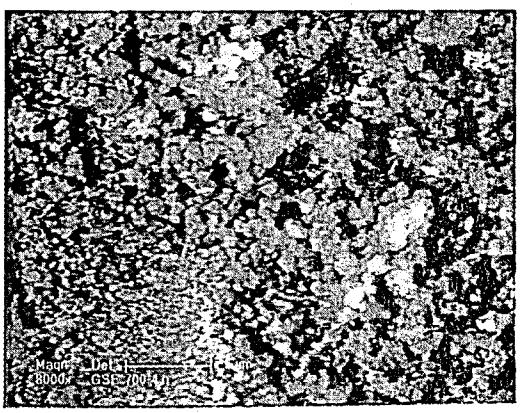


Figure 9.42. ESEM image of the sample calcined at 500°C for 4 hours



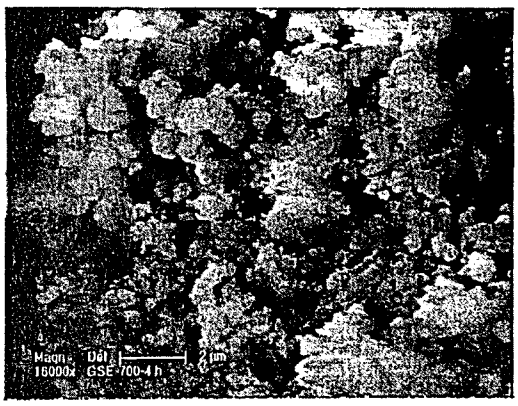


Figure 9.43. ESEM image of the sample calcined at 700°C for 4 hours

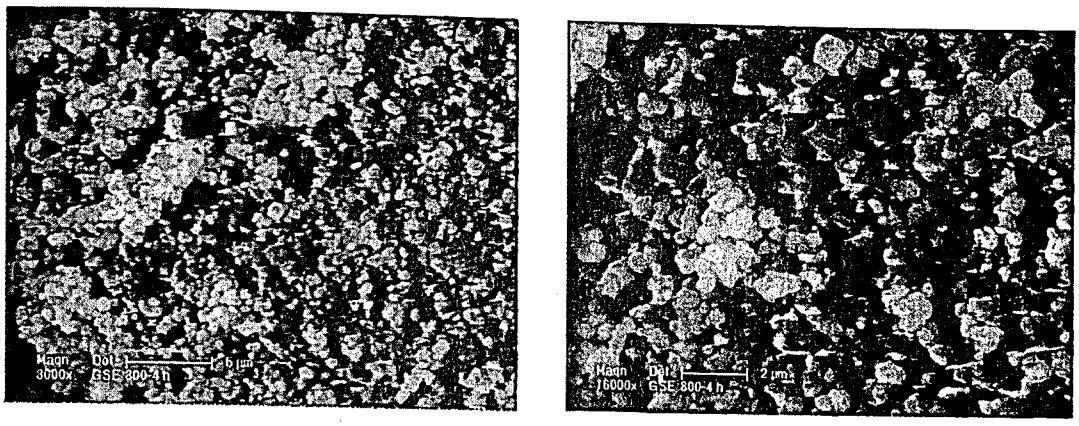


Figure 9.44. ESEM image of the sample calcined at 800°C for 4 hours

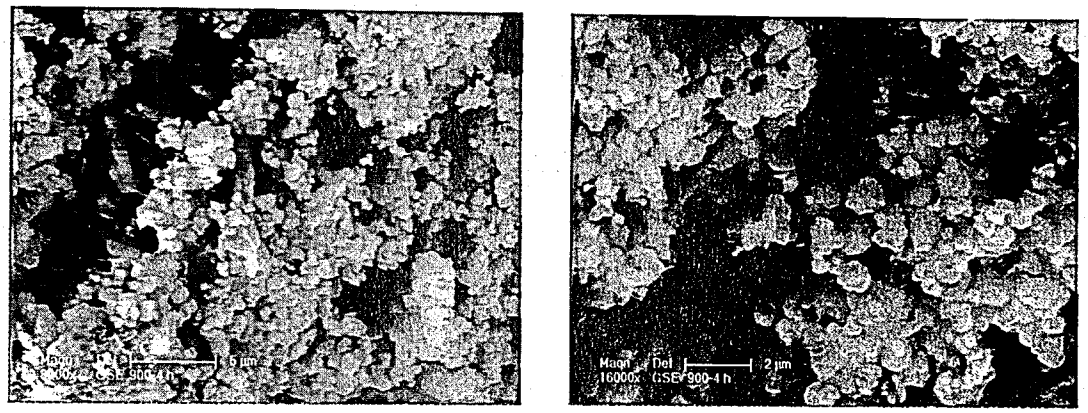


Figure 9.45. ESEM image of the sample calcined at 900°C for 4 hours

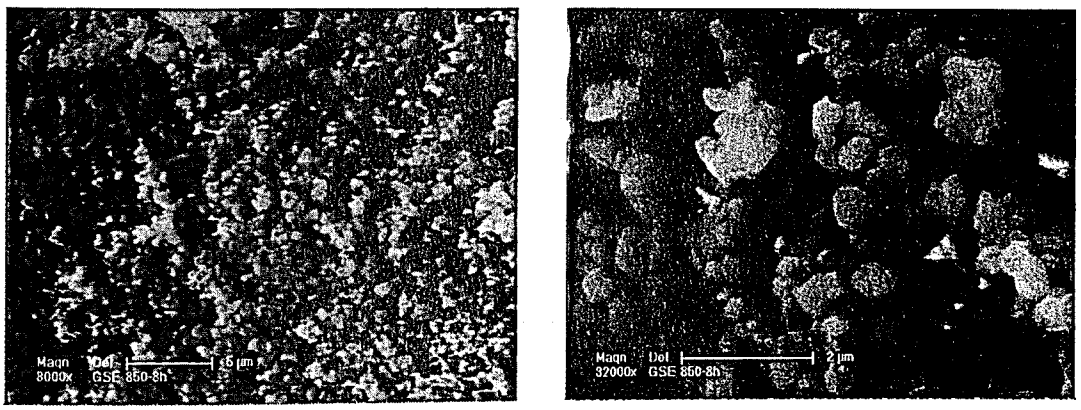


Figure 9.46. ESEM image of the sample calcined at 850°C for 8 hours

9.4. Effect of Grinding on the Particle Size Reduction and Surface Area

Reduction of the particle size increases the contact surface between the particles, and thus, leads to a better sintering behavior of the powder. To achieve this, the hydroxyapatite powder has been ground using a planetary ball mill by Fritsch GmbH, Germany. The grinding liquid was deionized water and the process took place at room temperature. The 500 ml alumina container of the ball mill has been filled with 33.33 % deionized water, 33.33. % hydroxyapatite powder and 33.33 % grinding balls by volume. 10 mm diameter alumina grinding balls are used and the ball mill is operated at half speed in order to prevent excessive wear of the grinding bowl and grinding balls.

Preliminary trials without any deflocculant have resulted in enormous coagulation due to the hydrophilic nature of hydroxyapatite. To prevent coagulation, 1 % polymethylmethacrylate has been added to the hydroxyapatite powder prior to grinding. Due to its polymeric nature polymethylmethacrylate decomposes at high sintering temperatures.

Particle size measurements have been taken prior to grinding and after 3 and 6 hours of grinding under the above mentioned conditions using a Malvern Instruments Mastersizer 2000.

Table 9.3. Effect of grinding on the particle size reduction of hydroxyapatite powder

	d (0.1) in μm	d (0.5) in μm	d (0.9) in μm
Particle Size of the Hydroxyapatite Powder prior to Grinding	13.974	206.691	566.044
Particle Size of the Hydroxyapatite Powder after 3 hours of Grinding	1.188	2.523	8.879
Particle Size of the Hydroxyapatite Powder after 6 hours of Grinding	0.131	1.727	5.276
Particle Size of Polymethylmethacrylate prior to Grinding	23.776	54.099	109.673

As seen in Table 9.3., even a short time of grinding has a significant effect on the particle size of the hydroxyapatite powder. After longer grinding times the particle size most obviously tends to saturate which is due to the nature of planetary ball milling. Although, the particle size after 6 hours is smaller than that after 3 hours grinding has been stopped after 6 hours to prevent excessive wear of the grinding bowl and balls which can result in impurities in the hydroxyapatite powder.

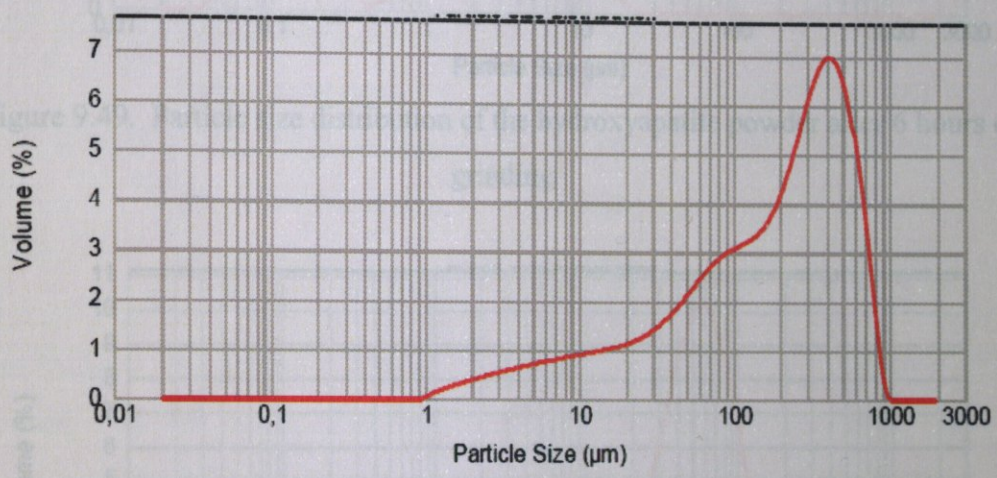


Figure 9.47. Particle size distribution of the hydroxyapatite powder prior to grinding

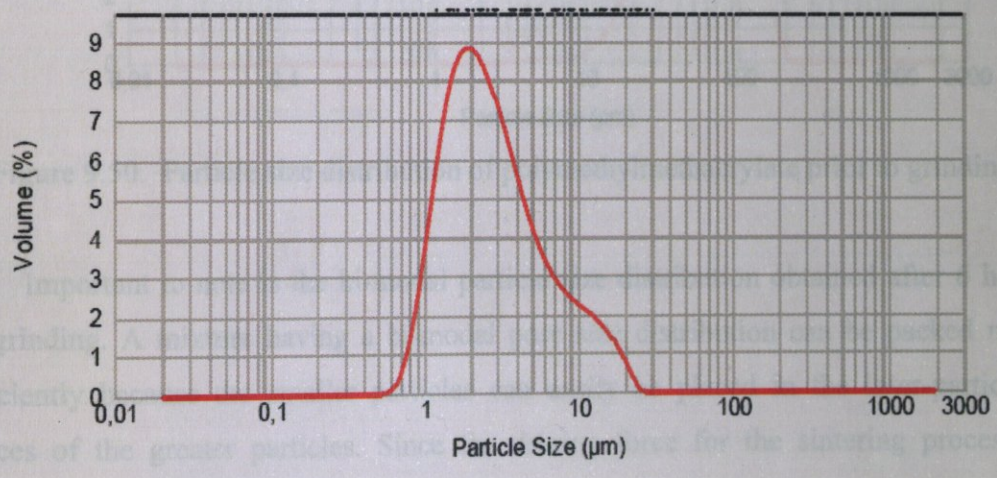


Figure 9.48. Particle size distribution of the hydroxyapatite powder after 3 hours of grinding

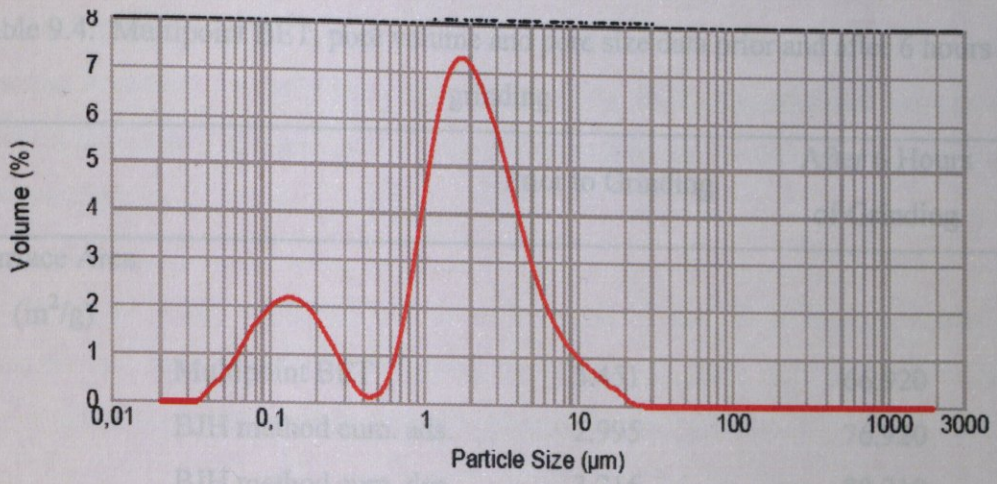


Figure 9.49. Particle size distribution of the hydroxyapatite powder after 6 hours of grinding

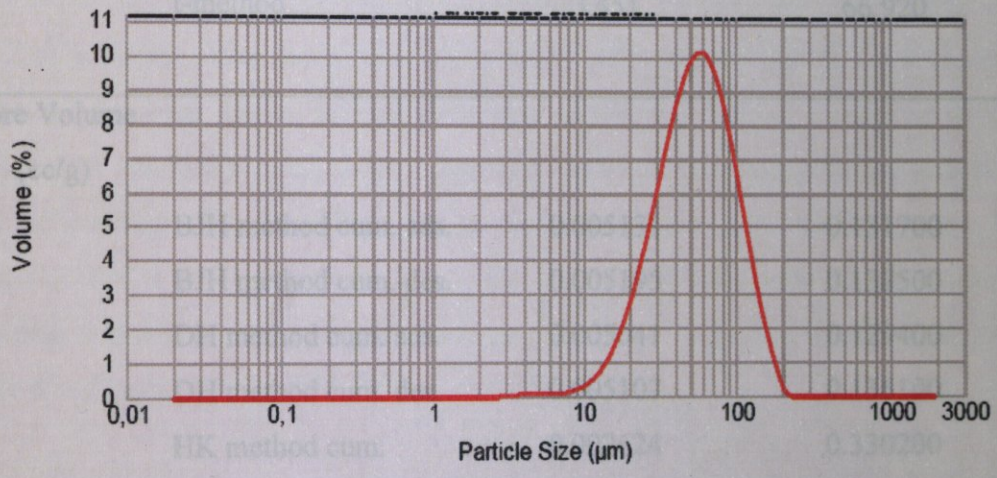


Figure 9.50. Particle size distribution of polymethylmethacrylate prior to grinding

Important to note is the bi-modal particle size distribution obtained after 6 hours of grinding. A mixture having a bi-modal pore size distribution can be packed more efficiently because the smaller particles can easily be placed in the inter-particular spaces of the greater particles. Since the driving force for the sintering process is primarily the surface tension an increased contact surface between the particles effects the sintering behavior of a powder mixture in a positive manner.

Table 9.4. Multipoint BET, pore volume and pore size data prior and after 6 hours of grinding

		Prior to Grinding	After 6 Hours of Grinding
Surface Area (m^2/g)			
	Multipoint BET	3.451	66.920
	BJH method cum. ads.	2.995	76.920
	BJH method cum. des.	3.216	80.210
	DH method cum. ads.	3.057	78.500
	DH method cum. des.	3.284	81.860
	t-method	3.451	66.920
Pore Volume (cc/g)			
	BJH method cum. ads.	0.005131	0.131700
	BJH method cum. des.	0.005195	0.138500
	DH method cum. ads.	0.005041	0.129400
	DH method cum. des.	0.005107	0.136100
	HK method cum.	0.002624	0.330200
	SF method cum.	0.002698	0.349100
Pore Size ($\overset{\circ}{A}$)			
	BJH method cum. ads.	16.130	16.280
	BJH method cum. des.	18.010	18.220
	DH method cum. ads.	16.130	16.280
	DH method cum. des.	18.010	18.220
	DA method cum.	9.100	9.600
	HK method cum.	8.981	9.012
	SF method cum.	15.730	15.780

Multipoint BET, pore volume and pore size data taken with a Nova 2200e Surface Area and Pore Size Analyzer prior and after grinding shows that grinding has a positive effect on the surface area and pore volume whereas pore size remains almost unchanged after grinding.

Previous works report surface areas between 60 and 70 m^2/g for synthetically produced and ball milled hydroxyapatite powders [32]. Ball milling apparently has similar effects on hydroxyapatite naturally obtained from fresh bone.

9.5. Production of Ceramic Structures from the Fine Hydroxyapatite Powder

Different amounts of polyvinylalcohol such as 1, 5 and 10 wt. % have been tried to act as a binder during sintering. However, after sintering at 1200 °C for 4 hours as a trial run it has been noticed that a high amount of polyvinylalcohol resulted in defected bodies. Not only surface cracks have been observed with increasing binder content but also hollow regions starting from the surface and reaching into the body have been formed. This is most obviously due to the fact that a large amount of an organic chemical acts as a porosifier and leaves large pores after burn out. Therefore, the binder content has been set as 1 wt. % for further experiments.

1 % stearic acid has been added to the hydroxyapatite powder to act as a lubricant during pressing and the inner walls of the die and the surface of the punch have been coated with pure vaseline in order to reduce the frictional forces during pressing. Trials without the application of vaseline have been resulted in samples with surface and edge cracks resulting from the improper distribution of the pressing forces in the sample during pressing.

The samples compacted using the 1 % polyvinyl alcohol as binder and 1 % stearic acid a s lubricant were more stable after pressing and did not show any surface defects after the sintering process.

9.6. Determination of the Effect of Sintering Time and Temperature on the Microstructure of the Fired Samples

In the experiment set designed to find out the effects of sintering time and temperature on the final product the inner wall of the die and the punch surface has been coated with pure Vaseline. Six samples containing binder and lubricant have been sintered in order to clarify the effect of sintering time and temperature on the final product and have been compared with the pure hydroxyapatite sample sintered at 1200 °C for 4 hours.

Table 9.5. Experiment set prepared to determine the effect of sintering time and temperature

Concentration of the Sintered Sample	Sintering Time (°C)	Sintering Temperature (hours)
99 % Hydroxyapatite + 1 % Polyvinyl Alcohol + 1 % Stearic Acid	1200	½
	1200	1
	1200	2
	1200	4
	1100	4
	1000	4
100 % Hydroxyapatite	1200	4

9.6.1. Effects of Sintering Time and Temperature on the Microstructure

The positive effect of temperature on sintering can be clearly observed on sampled sintered for 4 hours at temperatures 1000, 1100, and 1200 °C. Sintering is incomplete at 1000 but is obviously completed after 4 hours at 1200 °C. The time dependence of the sintering of hydroxyapatite is very clear. After 1 hour at 1200 °C sintering is still incomplete but reaches a complete state after 4 hours. The positive effect of stearic acid used as a lubricant and polyvinyl alcohol used as a binder can be seen on the images of the samples sintered with and without the additives at 1200 °C for 4 hours. Due to the

better lubrication and compaction effects the sample with the additives seem to have been better sintered after the same amount of time at the same sintering temperature. Resultingly, it can be concluded that stearic acid is a good compaction aid and polyvinylalcohol is good binder for hydroxyapatite.

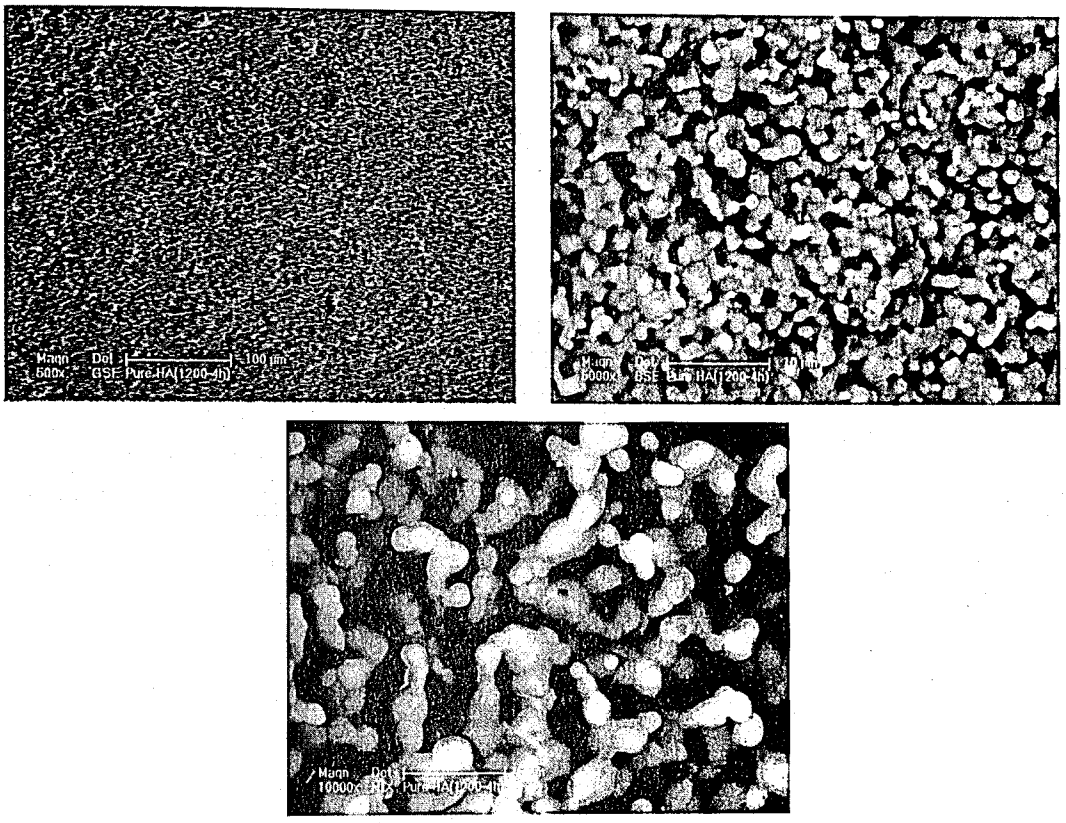


Figure 9.51. Pure hydroxyapatite sintered at 1200 °C for 4 hours

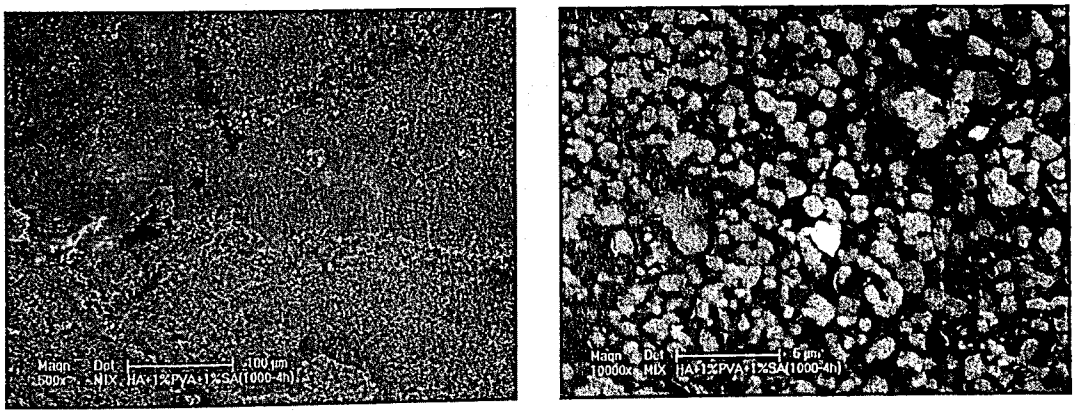


Figure 9.52. Hydroxyapatite + 1 % polyvinyl alcohol + 1 % stearic acid sintered at 1000 °C for 4 hours

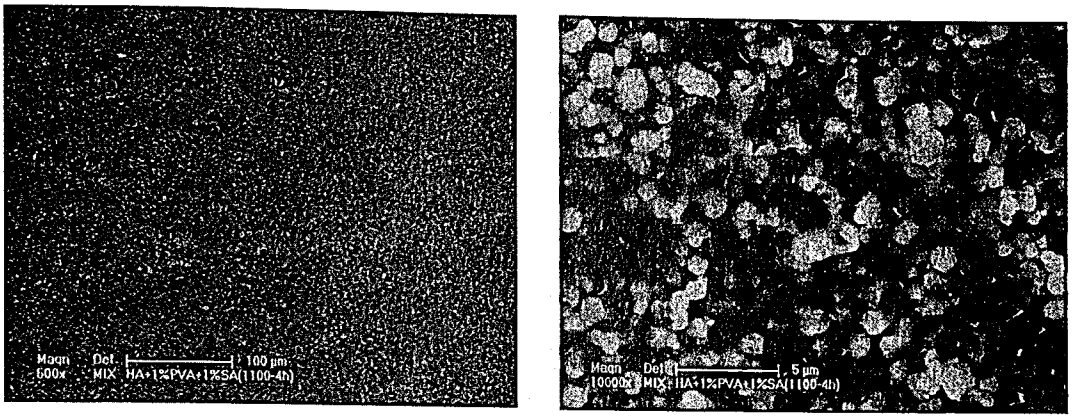


Figure 9.53. Hydroxyapatite + 1 % polyvinyl alcohol + 1 % stearic acid sintered at 1100 °C for 4 hours

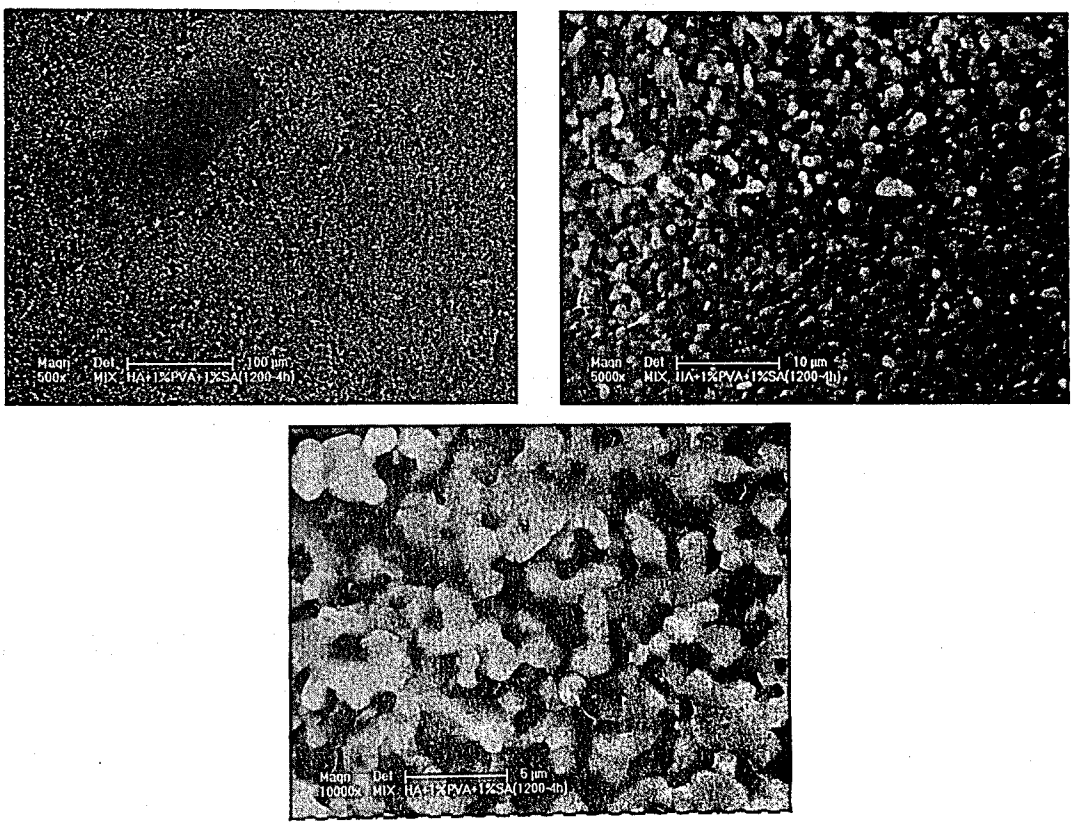


Figure 9.54. Hydroxyapatite + 1 % polyvinyl alcohol + 1 % stearic acid sintered at 1200 °C for 4 hours

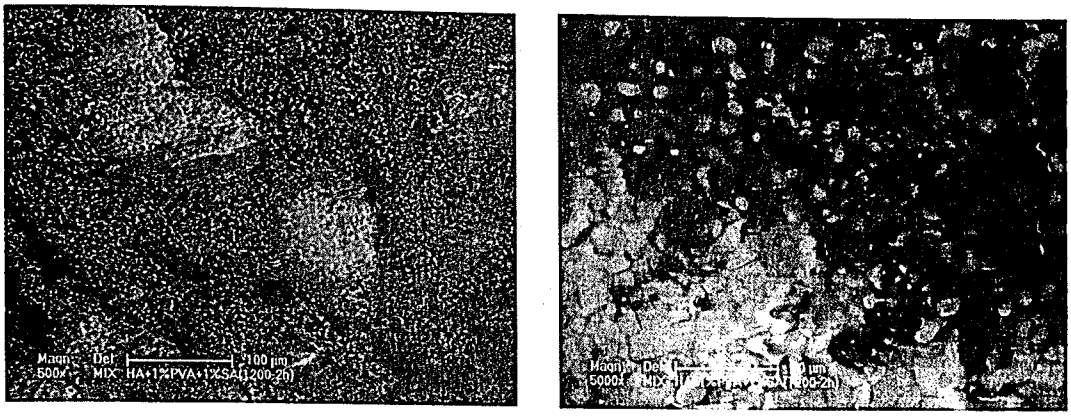


Figure 9.55. Hydroxyapatite + 1 % polyvinyl alcohol + 1 % stearic acid sintered at 1200 °C for 2 hours

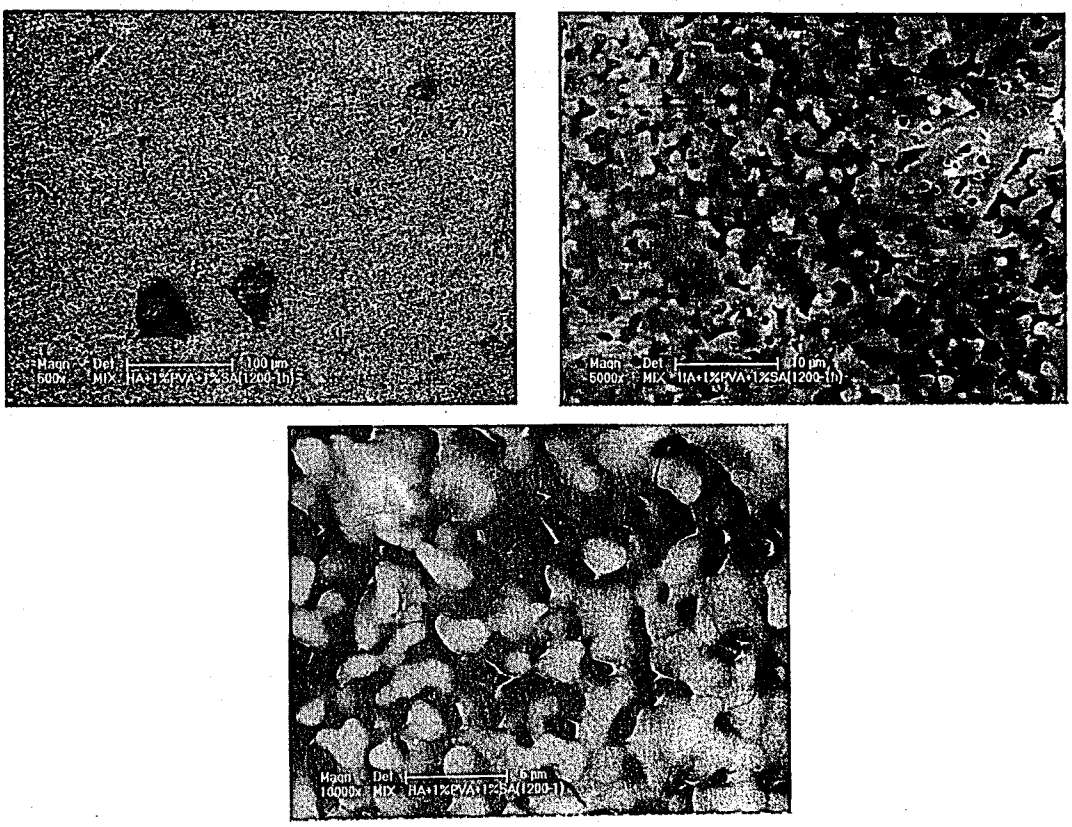


Figure 9.56. Hydroxyapatite + 1 % polyvinyl alcohol + 1 % stearic acid sintered at 1200 °C for 1 hour

9.6.2. Determination of the Effect of Boron Oxide (B_2O_3) as Sintering Additive

Five different batches containing 1 % polyvinyl alcohol as binder, 1 % stearic acid as lubricant and 1, 2, 5, 10, 20 % boron oxide as sintering additive have been prepared to investigate the effect of boron oxide on the sintering of hydroxyapatite. Samples have been sintered at 1200 °C for 4 hours using these batches. The positive effect of boron oxide as a sintering aid is clear starting from the composition of 1 % and becomes more obvious at 2 %. At higher concentrations boron oxide becomes dominant in the structure.

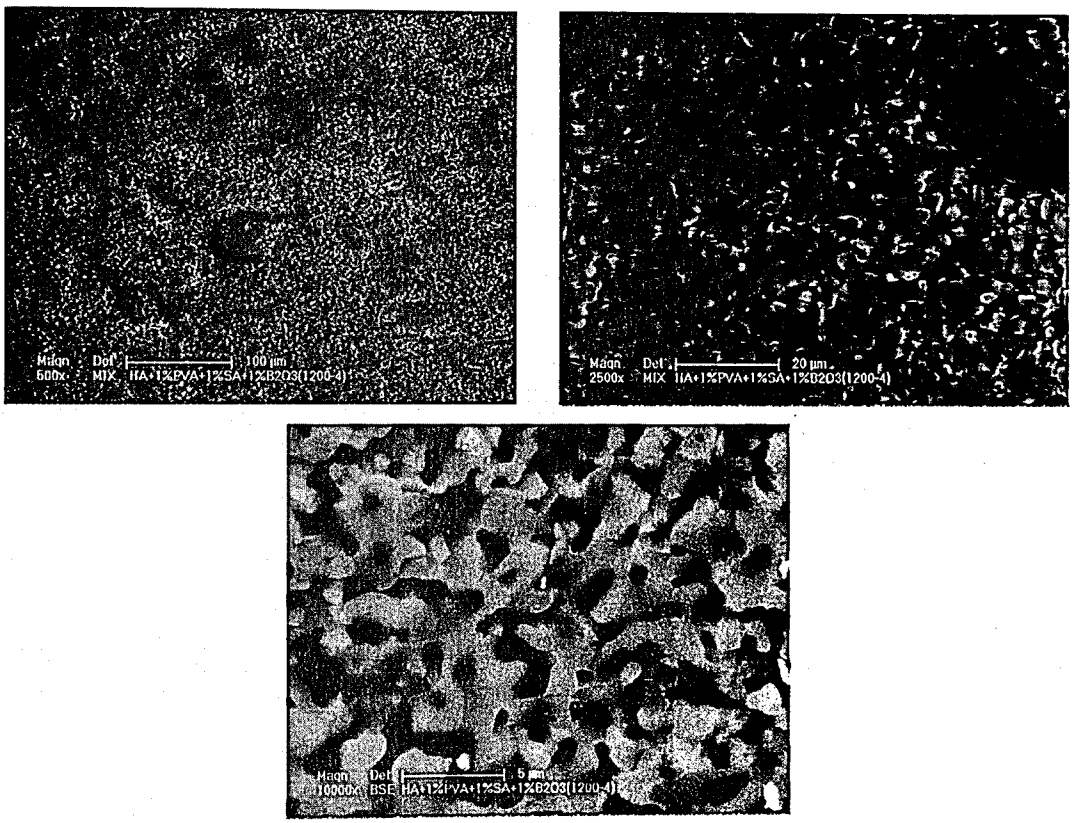


Figure 9.57. Hydroxyapatite + 1 % polyvinyl alcohol + 1 % stearic acid + 1 % boron oxide sintered at 1200 °C for 4 hours

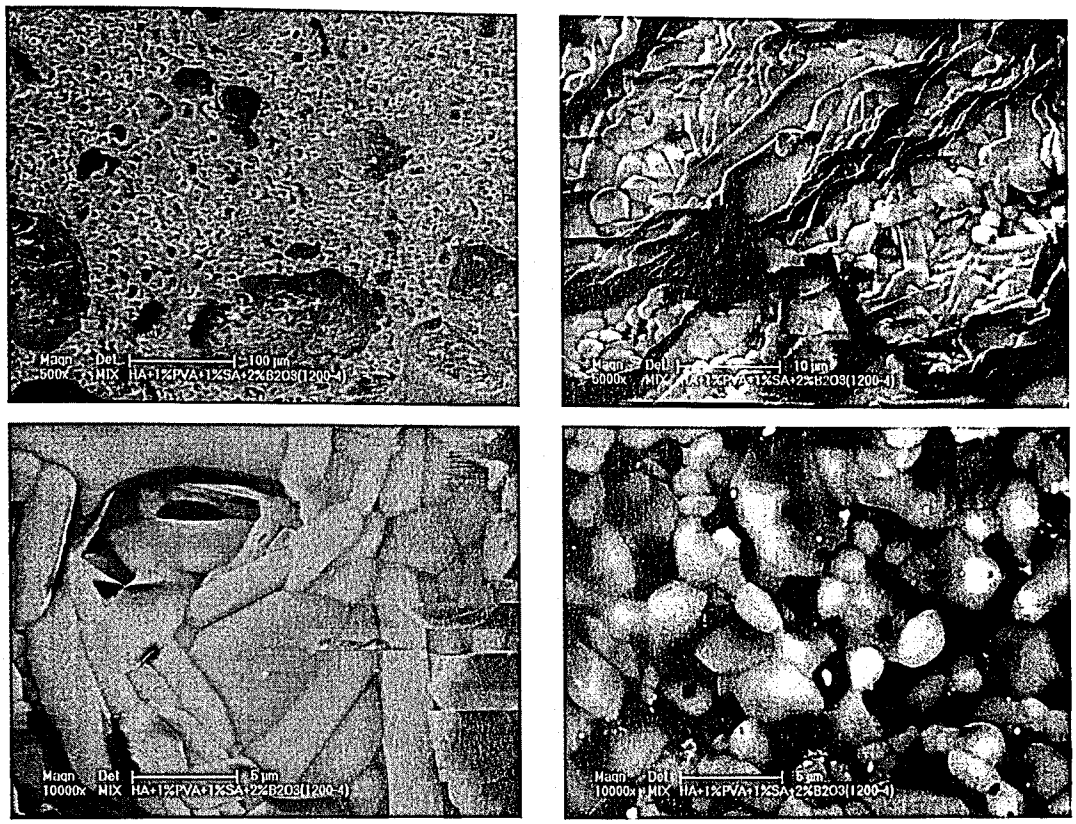


Figure 9.58. Hydroxyapatite + 1 % polyvinyl alcohol + 1 % stearic acid + 2 % boron oxide sintered at 1200 °C for 4 hours

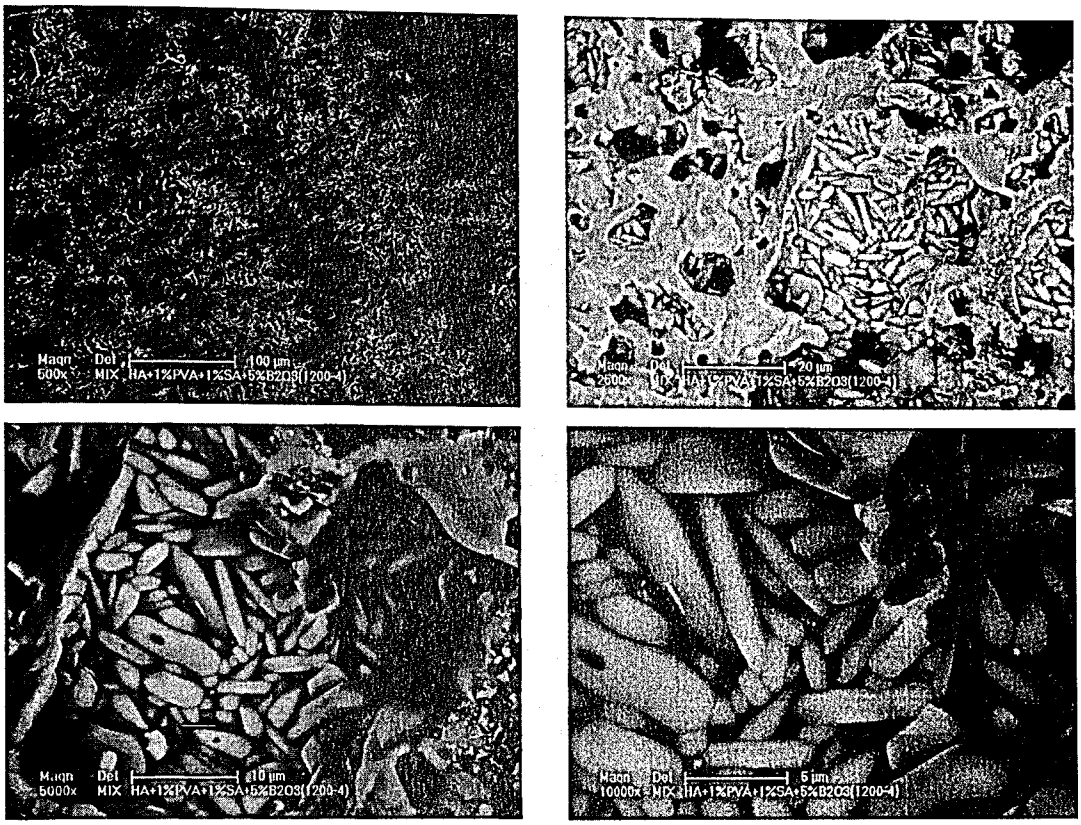


Figure 9.59. Hydroxyapatite + 1 % polyvinyl alcohol + 1 % stearic acid + 5 % boron oxide sintered at 1200 °C for 4 hours

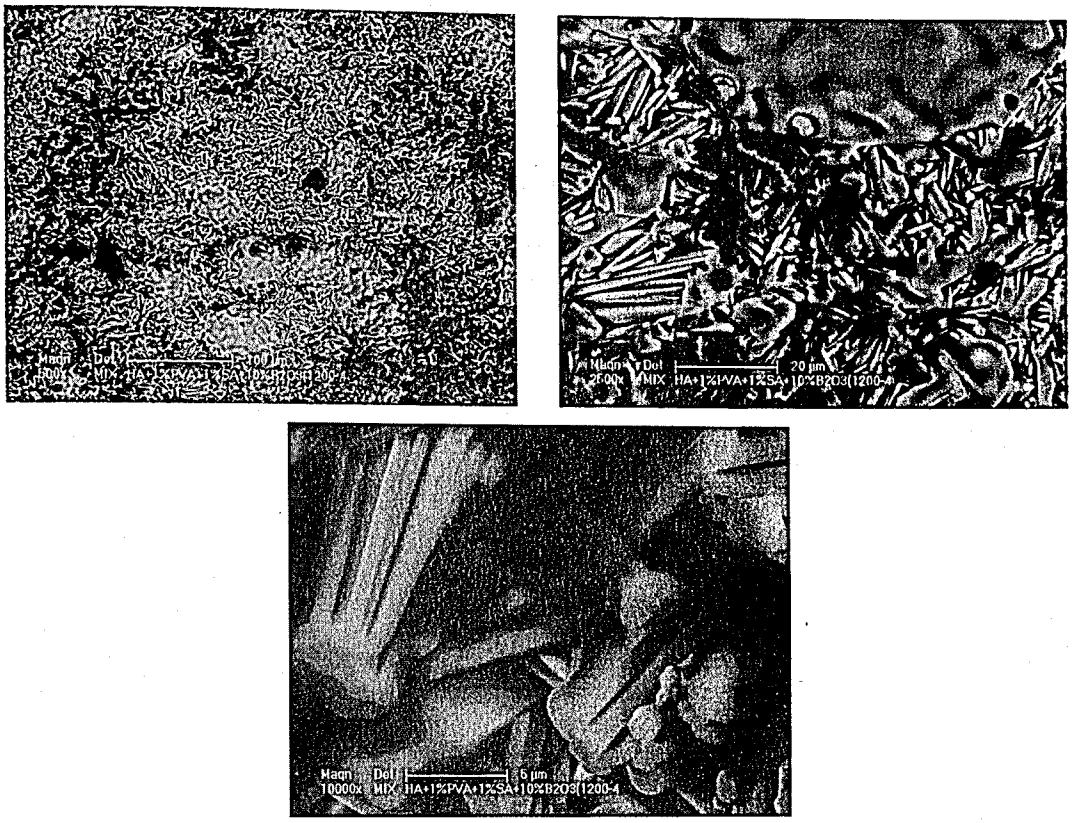


Figure 9.60. Hydroxyapatite + 1 % polyvinyl alcohol + 1 % stearic acid + 10 % boron oxide sintered at 1200 °C for 4 hours

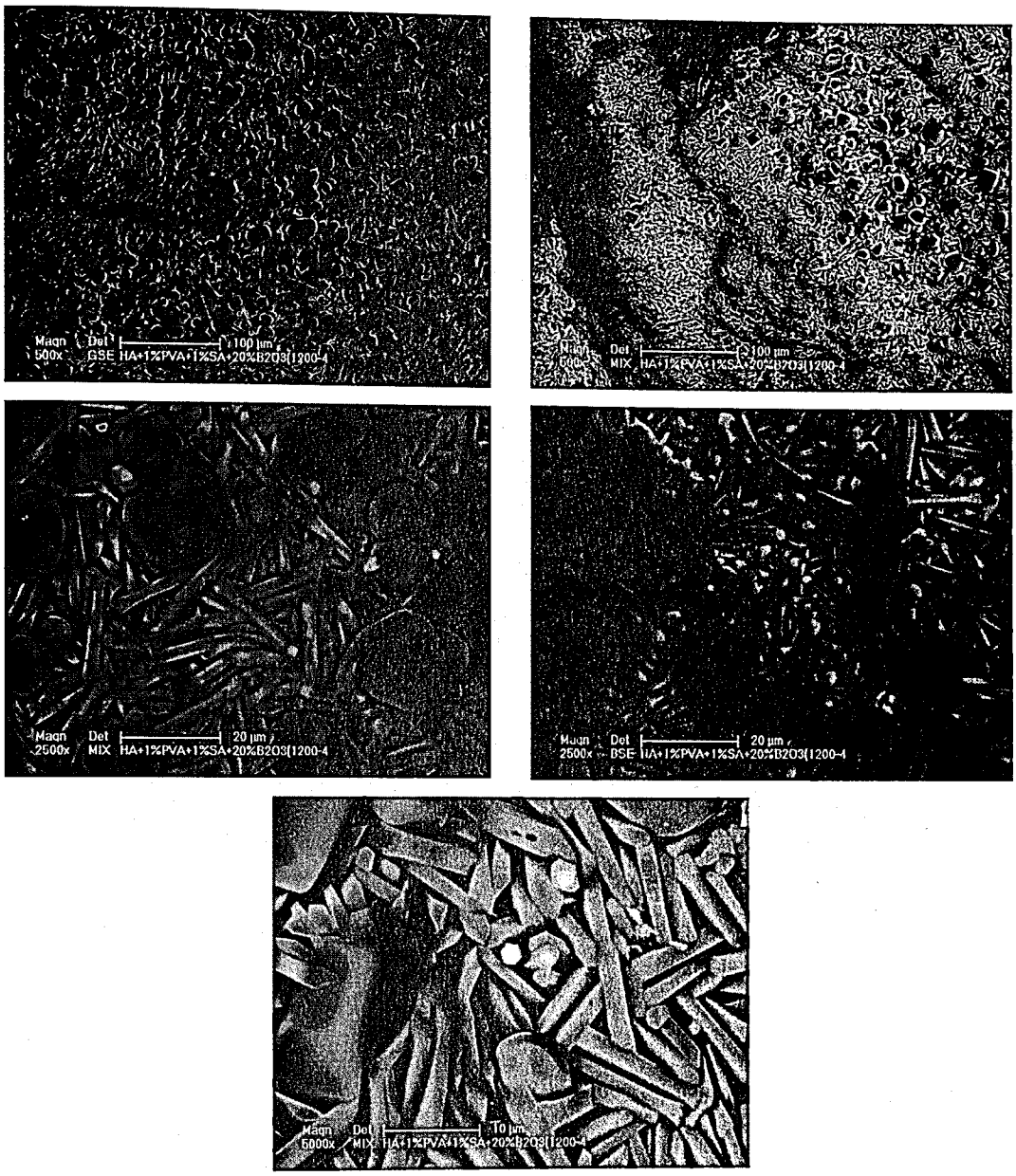


Figure 9.61. Hydroxyapatite + 1 % polyvinyl alcohol + 1 % stearic acid + 20 % boron oxide sintered at 1200 °C for 4 hours

10. CONCLUSIONS

Hydroxyapatite has been derived from the middle part of fresh calf femoral bones. The best suitable one among various methods involving degreasing in hexane, deproteinization in NaOH, and calcination for obtaining hydroxyapatite has been investigated. The most promising method has been found out to be calcination alone by comparing the per cent weight loss data, FTIR, X-Ray and EDAX measurements, and ESEM images of the hydroxyapatite powder produced by these methods. Calcination eliminates the entire organic fraction in the bone and excludes the danger of dissolution of hydroxyapatite and any ion exchange in a solution, like NaOH, used for deproteinization purposes.

The best suitable set of calcination time and temperature to remove the organic phase of bone has been determined and found out to be 8 hours and 850 °C, based on the % weight loss, EDAX, and ESEM data.

The produced hydroxyapatite has been wet ball milled and the effect of milling time on reducing of particle size has been investigated through particle size measurements. 6 hours of ball milling has resulted in an average particle size of 5 μm and in an increase of the surface area to 70 m^2/g. These values are comparable to hydroxyapatite sample found in the literature.

To further investigate the effect of reducing the particle on the sintering characteristics of hydroxyapatite the milled fine hydroxyapatite powder has been sintered at 1000, 1100, and 1200 for ½, 1, 2 and, 4 hours with addition of 1 % of polyvinylalcohol as binder and 1 % of stearic acid as lubricant and the differences have been compared with a pure hydroxyapatite sample via EDAX measurements and ESEM images. It has turned out to be that sintering at 1200 °C for 4 hours leads to the best results among the possibilities based on ESEM and that polyvinyl alcohol is a suitable binder and stearic acid is a good compaction aid for hydroxyapatite.

Since boron is known to induce bone growth and the hydroxyapatite ceramics produced in this work are considered for biomedical applications experiments with 1, 2, 5, 10, and 20 % of boron oxide additions have been conducted to investigate the effect of boron oxide on the sintering characteristics of hydroxyapatite. For this purpose 5 batches with the stated concentrations have been sintered at 1200 °C for 4 hours and it has been found out that boron oxide has a positive effect on sintering of hydroxyapatite due to the wet sintering effect. Based on the observation of the ESEM images 2 % boron oxide has given the best results regarding the sintering of hydroxyapatite.

APPENDIX A: A BRIEF HISTORY OF CERAMIC TECHNOLOGY

Hand mixing, hand building, and scratch and slip decorating of earthenware date back to before 5000 BC. The first forming machine was probably the potter's wheel, which was used earlier than 3500 BC for throwing a plastic earthenware body and later for turning a somewhat dried, leather, hard body. Shaping by pressing material in fired molds and firing in a closed kiln were subsequent developments [23].

The most notable achievement early in the Christian era was the development in China of pure white porcelain of high translucency. Duplication in the West was frustrated until 1708, when a young German alchemist, Fredrich Bottger, under the direction of the celebrated physicist Count von Tschirnhaus, discovered that fine porcelain could be produced on firing a body containing a fire-resistant clay with fusible materials. Other inventions in the 18th century included the use of a template for forming, slip casting in porous molds, auger extrusion, transfer decoration, and firing in a tunnel kiln [23].

The introduction of steam power in the 19th century led to the mechanization of mixing, filter pressing, dry pressing, and pebble mill grinding. Near the end of that century, separate phases of silica were distinguished using optical microscopy, and silicon carbide was synthesized in an electric furnace. Pyrometric cones were developed by Seager to control firing [23].

The first half of the 20th century saw the rapid development of x-ray techniques for the analysis of the; atomic structure of crystals and later electron microscopy for examining microstructure beyond the limit of the optical microscope. Material systems became more refined, and special compounds were developed, synthesized, and fabricated into products for refractory and electronic applications. Refined organic additives were purposefully introduced to improve the processing behavior. Industrial production became mechanized, and several stages of manufacturing were automated. Thermocouples were used routinely to monitor temperatures during firing [23].

The second half of the 20th century has witnessed major advances in the synthesis, characterization, and fabrication of ceramic products. Scanning electron microscopy is now used for routine microstructural analysis for quality control in manufacturing. Several different instrumented techniques have been developed for bulk chemical analysis at a concentration of less than a fraction of one part in a million and surface concentrations a few atomic layers in thickness. The particle size distributions of a material can be determined to below 0.1 μm in a few minutes. The flow behavior during forming is developed and controlled using a multicomponent system of additives. Testing apparatus and processing machinery are much more advanced. Computers are; now used throughout the industry to monitor and/or control raw-material handling and preparation, fabrication, and firing [23].

A.1. Industrial Ceramic Processing

Ceramic processing commonly begins with one or more ceramic materials, one or more liquids, and one or more special additives called processing aids. The starting materials or the batched system may be beneficiated chemically and physically using operations such as crushing, milling, washing, chemical dissolving, settling, flotation, magnetic separation, dispersion, mixing, classification, de-airing, filtration, and spray-drying. The forming technique used will depend on the consistency of the system (i.e. , slurry, paste, plastic body, or a granular material) and will produce a particular unfired shape with a particular composition and microstructure. Drying , removes some or all of the residual processing liquids. Additional operations include green machining, surface grinding, surface smoothing and cleaning, and the application of surface coatings such as electronic materials or glaze. The finished material is then commonly heat-treated to produce a sintered microstructure. The sintered product may be a single component or a multicomponent composite structure. A general processing flow diagram indicating the sequences of operations used in forming a product is shown in Figure A.1. [23].

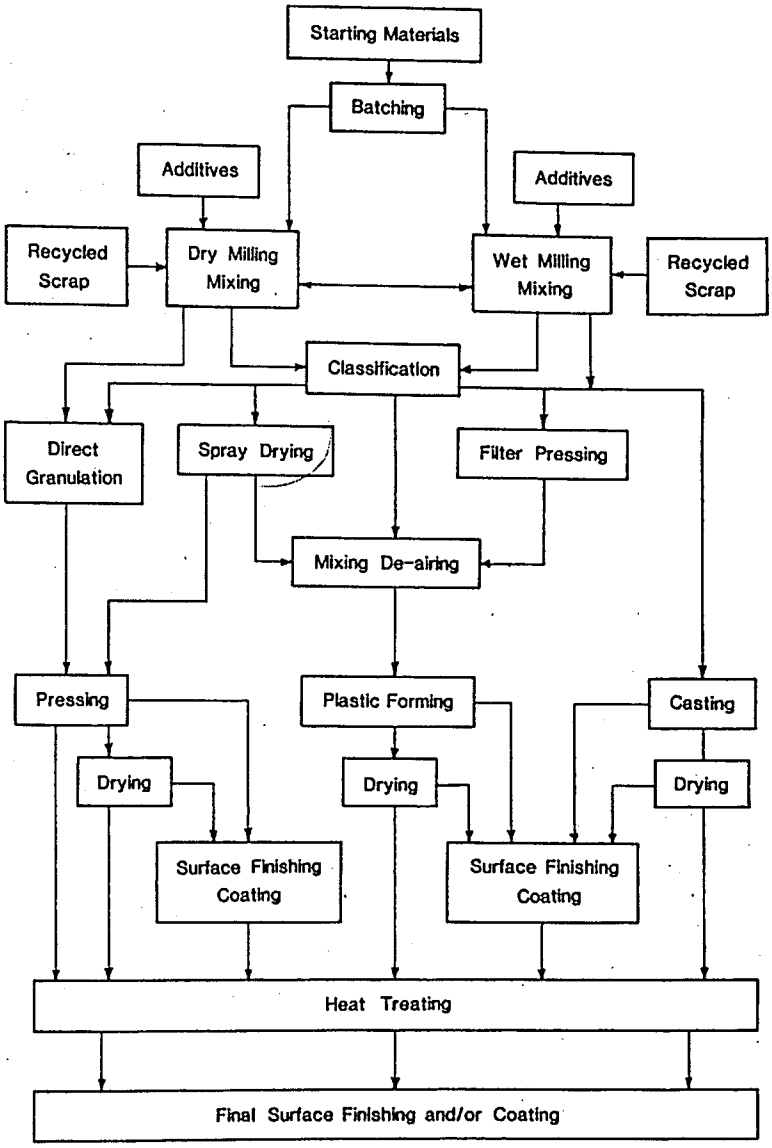


Figure A.1. A General processing flow diagram illustrating processing paths from raw materials to the fired product [23]

A.2. Science in Ceramic Processing

Before the development of scientific insights of ceramic processing, the properties of the product were often correlated with changes in a processing operation to identify the more important superficial variables. This empirical approach is still used and can be aided greatly using computers and statistical programs. However, empirical correlations such as these do not provide a scientific understanding of the fundamental causes of behavior during processing and forming. The probability that adjustments

based on empirical correlations alone will produce significant advances is small, because the potential number of unsuccessful combinations of variables is always relatively large. Also, empirical correlations may be of little heuristic value when the processing engineer is faced with a lack of reproducibility in manufacturing, an insufficient reliability in the performance of nominally identical products, or the development of new products [23].

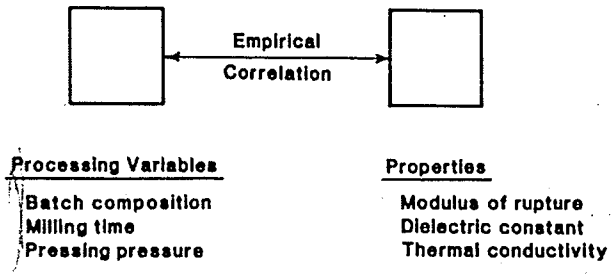


Figure A.2. Correlation between the final properties and processing variables may identify the more sensitive processing parameters but is empirical [23]

Viewed as a science, ceramic processing is the sequence of operations that purposefully and systematically changes the chemical and physical aspects of structure, which we call the characteristics of the system. The properties at each stage are a function of the characteristics of the system at each stage and the ambient pressure and temperature, as is shown in the below figure.

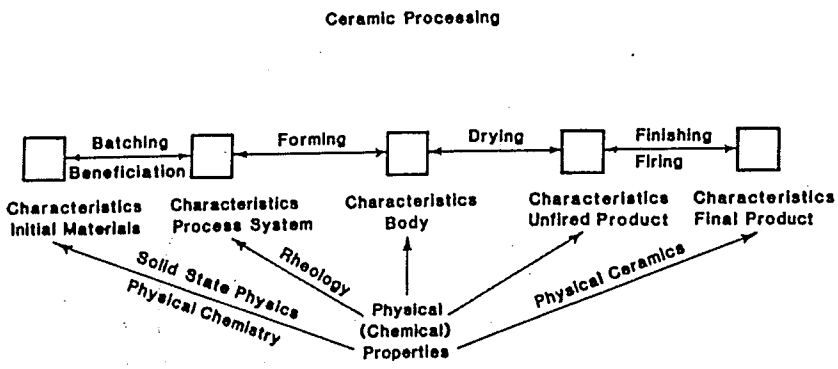


Figure A.3. Processing develops the characteristics of the system [23]

The objectives of the science of ceramic processing are to identify the important characteristics of the system and understand the effects of processing variables on the evolution of these characteristics. The objectives in process engineering should be to change these characteristics purposefully to improve product quality. Because of the key dependence on controlling characteristics, an understanding of techniques for characterizing the starting materials and the process system at each stage is an integral part of any discussion of ceramic processing [23].

Raw materials are now more beneficiated, more consistent, and often, much simpler in composition. Modern instrumentation for analyzing ceramics materials and systems is more automated and precise, and with microcomputer accessories quantitative data are obtained quickly and presented in a convenient format. Computer-controlled, closed, raw material handling systems improve the precision, efficiency, health, and safety in batching and mixing particulate materials. The processing pressure and temperature are more precisely monitored and controlled. Wear-resistant materials are used in critical areas to minimize maintenance and contamination. In the factory, on-line monitoring and control of production processes is practiced in some stages of processing in some industries [23].

Principles of processing science can provide insights into fundamental causes of behavior, procedures for modifying and controlling materials and processes, and avenues for improving manufacturing productivity. The role of ceramic processing science in ceramic manufacturing will surely increase [23].

APPENDIX B: PROPERTIES OF BONE

B.1. Bone as a Living Tissue

Bone is a specialized form of a connective tissue forming the skeleton of most vertebrates and consisting of cells in an intercellular substance. It differs from other connective tissues in its hardness. Hardness of bone results from deposition of a complex mineral substance within a soft organic matrix. Therefore, bone is an organic composite of ceramic in an organic matrix.

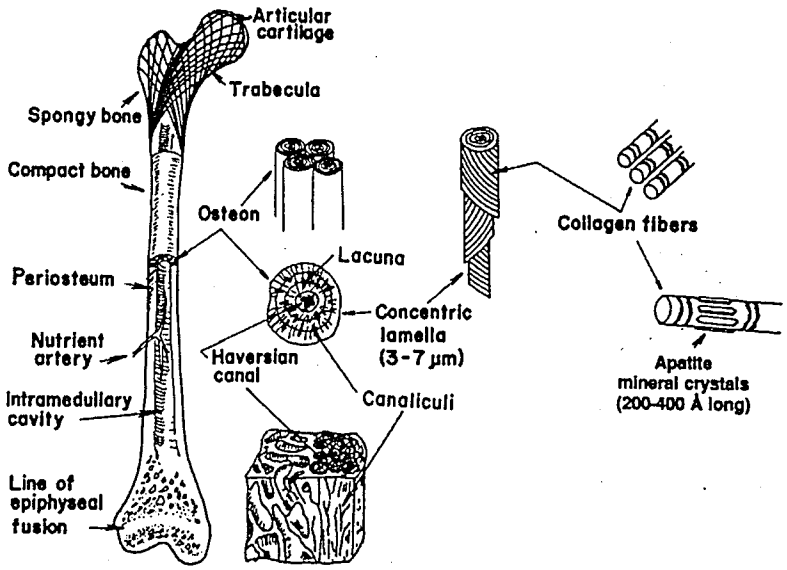


Figure B.1. Organization of a typical bone [11]

The interstitial substance, which is calcified, has a fibrillar structure similar to that of connective tissue. The fibers are mainly those of collagen. The ground substance, as in connective tissue, composes mostly of mucopolysaccharides [46].

The mineral phase of bone composes mostly of calcium, phosphate and citrate. These minerals are produced by the cells which are specialized forms derived from cells common to connective tissue [46].

The organic fraction, of which only a small portion is bone cells, makes up almost 25 % of the weight of the bone. 10 % of the total weight of bone is water whereas the remaining 65 % of bone weight is the bone mineral [21].

Bones being part of the skeleton have several important functions throughout the organism. These are [49]:

Support: The skeleton consisting of bones provides a hard framework upon which many organs are attached and which supports the whole body.

Protection: Parts of the skeleton protects the inner organs, e.g. the skull protects the brain, the vertebrae surround the spinal cord and the rib cage protects and supports lungs and heart.

Movement: Skeletal muscles attached to the bones by tendons simply use the bones in the extremities as levers to move the body and its parts.

Blood cell formation: Most of the blood cell formation (hematopoiesis) takes place within the marrow cavities of certain bones.

Mineral storage: Bones serve as a reservoir for many minerals of which most important ones are calcium and phosphate. The minerals stored in bones can be released into the blood stream as ions and distributed to all body parts whenever the need arises. The storage and withdrawal of minerals to and from the bone is a continuous process and takes place throughout the whole life of the organism.

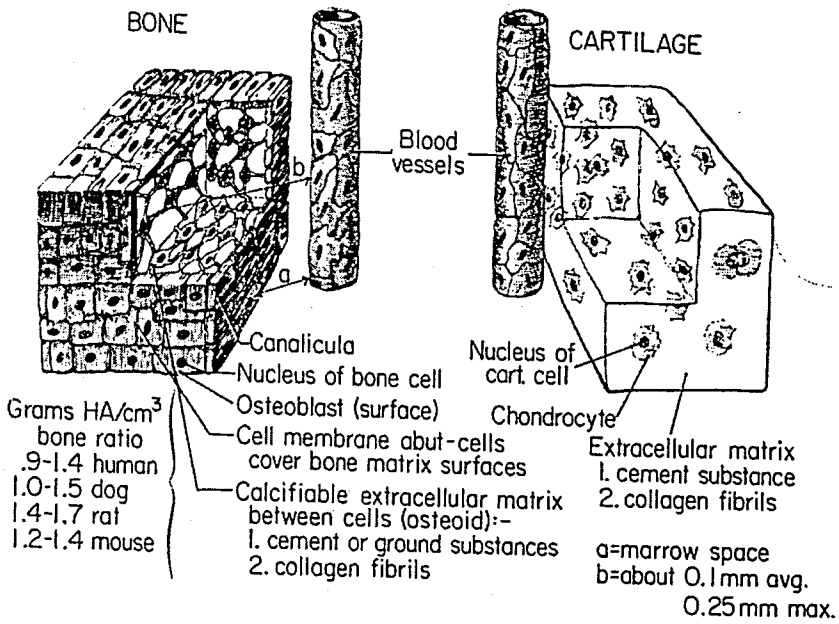


Figure B.2. A diagrammatic view of bone [46]

B.2. Bone Cells

There are three types of bone cells with different functions. Osteoblasts are associated with formation of bone whereas osteocytes with the maintenance of bone as a living tissue. On the other hand, osteoclasts have the function of resorption of bone. These cells working in close cooperation with each other maintain the overall functionality of bone in a continuous formation and resorption mechanism.

B.3. Organic Portion of Bone

The intercellular portion of the bone consists of the organic matrix, the inorganic part which is the mineral of bone and water. The organic matrix itself is composed of collagen fibers and the ground substance.

Collagen, occurring in fibrils with double cross-banding at average intervals of 64 nm, makes up 90-96 % of the organic portion of the bone. Chemically, it is characterized by a low content of aromatic amino acids and a high content of pyrrolidine amino acids and glycine. The collagen fibrils are 0.3-0.5 μm in diameter and they are arranged in small bundles which are 3-5 μm thick [46].

Ground substance is chemically characterized by sulfated polysaccharides which contain hezoamines and amino sugars. Ground substance is thought to be related to the calcification process [46].

Water is considered to have the primary function to provide space for further calcification. While the organic matter of normal compact bone remains constant in relation to volume calcification of bone occurs by the replacement of water by crystals of bone mineral. The space available for mineral is the greater part of that occupied by water. Calcification and crystal growth proceed until there is no space left for further expansion [46].

B.4. Inorganic Portion of Bone

Inorganic portion of the bone makes up almost two-thirds of the weight of the bone which corresponds to half of its volume

The crystals of the bone mineral are microscopic in size. The bone salt is not a single, homogenous chemical. Its basic atomic structure is close that of an apatite which is called hydroxyapatite with the approximate formula of $Ca_{10}(PO_4)_6(OH)_2$ [21]. The chemical composition of the fraction is less clearly define, partly because of its variability and partly because of the difficulty of differentiating between the constituents of the basic structure, the ions having only a surface relationship to the crystals and those possibly admixed with the apatite crystals in a separate phase. However, in general, the inorganic portion of bone consists of Ca^{2+}, PO_4^{3}, OH^-, CO_3^{2-} and citrate. There are also some other ions like Na^+, Mg^{2+} and F^- in small amounts. Various substitutions and exchanges of ions occur in the crystal structure. The minute crystals and the voids and discontinuities in their structure expose large surfaces to the fluids of the body and the ions held by adsorption or by substitution at these surfaces, as well as those incorporated within surface unit cells with unshared sides, have a considerable influence upon the total composition of the mineral. The surface ions are subject to rapid exchange with the fluids bathing the crystals because dissolution and recrystallization may occur. The reactivity of the mineral varies with its age, its immediate environment and with its structure and chemical composition.

Table B.1. Composition of dry, fat-free, bovine cortical bone [46]

		Per cent	mEq / g
Cations			
	Calcium	26.70±0.02	13.32±0.01
	Magnesium	0.436±0.009	0.358±0.008
	Sodium	0.731±0.015	0.318±0.007
	Potassium	0.055±0.0009	0.014±0.0002
	Total		14.01
Anions			
	Phosphorus	12.47±0.013	-
	as PO_4^{3-}	-	12.06±0.012
	Carbon dioxide	3.48±0.022	-
	as CO_3^{2-}	-	1.58±0.010
	Citric acid	-0.363±0.004	-
	as Cit^{3-}	-	0.135±0.0006
	Chloride	0.077±0.004	0.022±0.001
	Fluoride	0.072±0.003	0.037±0.002
	Total		13.83
(mEq cations) / (mEq anions)			1.012
(mM Ca) / (mM P)			1.656

The crystals may be visualized as rod-like with diameters of about 50 $\mathring{A}$ and composed of chains of microcrystals arranged end to end. These chains are often 200 $\mathring{A}$ long, oriented in the long axis of the collagen fibrils and possessing a special relationship to their cross-banding. Some of the crystals are also prism-like with the smallest dimension of the order of 20-30 $\mathring{A}$. [46-48]

B.5. Bone as a Composite Material

Bone can be considered as a composite material of collagen and hydroxyapatite. Apatite crystals are very stiff and strong. As a successful composite material, the bone's strength is higher than that of either apatite or collagen, because the softer component prevents the stiff one from brittle cracking, while the stiff component prevents the soft one from yielding.

On the other hand, bone is also a smart material by showing functional adaptation properties. In this way, bone adapts itself to a function by making use of it. Functional stimuli trigger a quantitative self-regulation mechanism in the bone [47].

B.6. Mechanical Properties of Bone

Bone is hard material and its stress-strain behavior is similar to those of many engineering materials. Dry bone is brittle and fails at a strain of 0.4 % whereas wet bone fails at 1.2 %.

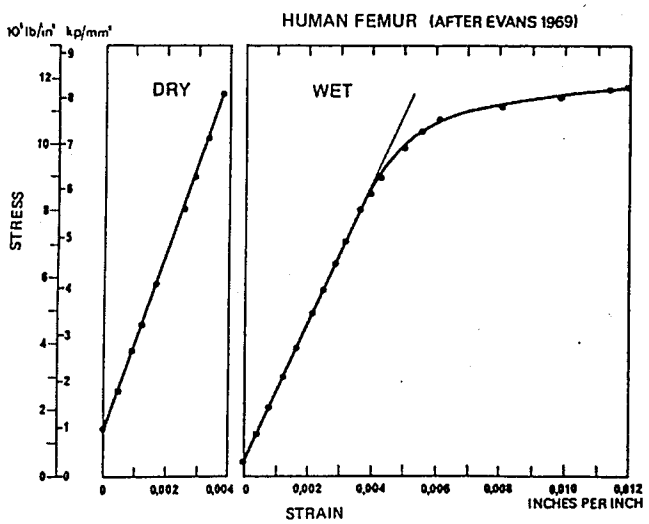


Figure B.3. Stress-strain curves of human femoral bone [47]

The strength of bone varies with age, sex, nutrition and living conditions. Resulting from the inhomogenous anisotropic composite nature of the bone, the strength also depends on the testing conditions such as orientation of the load, the strain rate and whether it is dry or wet.

Table B.2. Mechanical properties of wet compact bone in tension, compression, and torsion parallel to axis [47]

Bone	Horses	Cattle	Pigs	Human (20-39 yrs)
		Ultimate Tensile Strength (MPa)		
Femur	121±1.8	113±2.1	88±1.5	124±1.1
Tibia	113	132±2.8	108±3.9	174±1.2
Humerus	102±1.3	101±0.7	88±7.3	125±0.8
Radius	120	135±1.6	100±3.4	152±1.4
		Ultimate Percentage Elongation		
Femur	0.75±0.008	0.88±0.020	0.68±0.010	1.41
Tibia	0.70	0.78±0.008	0.76±0.028	1.50
Humerus	0.65±0.005	0.76±0.006	0.70±0.033	1.43
Radius	0.71	0.79±0.009	0.73±0.032	1.50
		Modulus of Elasticity in Tension (GPa)		
Femur	25.5	25.0	14.9	17.6
Tibia	23.8	24.5	17.2	18.4
Humerus	17.8	18.3	14.6	17.5
Radius	28.8	25.9	15.8	18.9
		Ultimate Compressive Strength (MPa)		
Femur	145±16	147±1.1	100±0.7	170±4.3
Tibia	163	159±1.4	106±1.1	
Humerus	154	144±1.3	102±1.6	
Radius	156	152±1.5	107±1.6	

Table B.2. Mechanical properties of wet compact bone in tension, compression, and torsion parallel to axis [47] (Cont.)

Bone	Horses	Cattle	Pigs	Human (20-39 yrs)
		Ultimate Percentage Contraction		
Femur	2.4	1.7±0.02	1.9±0.02	1.85±0.04
Tibia	2.2	1.8±0.02	1.9±0.02	
Humerus	2.0±0.03	1.8±0.02	1.9±0.02	
Radius	2.3	1.8±0.02	1.9±0.02	
		Modulus of Elasticity in Compression (GPa)		
Femur	9.4±0.47	8.7	4.9	
Tibia	8.5		5.1	
Humerus	9.0		5.0	
Radius	8.4		5.3	
		Ultimate Shear Strength		
Femur	99±1.5	91±1.6	65±1.9	54±0.6
Tibia	89±2.7	95±2.0	71±2.8	
Humerus	90±1.7	86±1.1	59±2.0	
Radius	94±3.3	93±1.8	64±3.2	
		Torsional Modulus of Elasticity (GPa)		
Femur	16.3	16.8	13.5	3.2
Tibia	19.1	17.1	15.7	
Humerus	23.5	14.9	15.0	
Radius	15.8	14.3	8.4	

The effect of anisotropy is expected since the osteons which are fiber-like structures found in compact bone are arranged in longitudinal direction. Therefore, the Young's Modulus and the tensile and compressive strengths in the radial or tangential direction are approximately 2 and 1.5 times higher than those in the radial or tangential directions, respectively.

The effect of loading also plays a significant role in determining the strength of bone. Thus, bone shows a viscoelastic behavior. Young's Modulus, ultimate compressive and yield strength increase with increased rate of loading whereas the failure strain and the fracture toughness of the bone reach a maximum and then decrease indicating that there is a critical rate of loading.

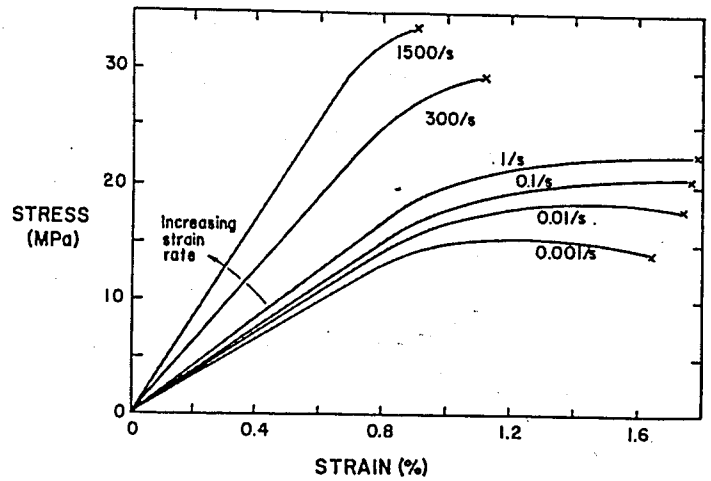


Figure B.4. Stress as a function of strain and strain rate for human compact bone [1]

Mineral content of a particular bone effects its strength. Highly mineralized bone has a higher modulus of elasticity and bending strength but lower toughness. This indicates the importance of the organic phase in providing toughness and energy absorption capabiiity in bone.

Table B.3. Properties of three different bones with varying mineral contents [1]

Type of bone	Work of fracture (J/m^2)	Bending strength (MPa)	Young's Modulus (GPa)	Mineral content (wt. %)	Density (g/cm^3)
Deer antler	6190	179	7.4	59.3	1.86
Cow femur	1710	247	13.5	66.7	2.06
Whale tympanic bulla	200	33	31.3	86.4	2.47

REFERENCES

1. Park, J. B., and R. S. Lakes, *Biomaterials: An Introduction*, John Wiley & Sons, New York, 1992.

2. Ratner, B. D., A. S. Hoffman, F. J. Schoen, and J. E. Lemons (Editors), *An Introduction to Materials in Medicine*, Academic Press, New York, 1996.

3. Vail, N. K., L. D. Swain, W. C. Fox, T. B. Lee, G. Aufdlemorte, and J. W. Barlow, "Materials for Biomedical Applications", *Materials and Design*, Vol. 20, pp. 123-132, 1999.

4. Joschek, S., B. Nies, R. Krotz, and A. Göpferich, "Chemical and Physicochemical Characterization of Porous Hydroxyapatite Ceramics Made of Natural Bone", *Biomaterials*, Vol. 21, pp. 1645-1658, 2000.

5. Sykaras, N., A. M. 'lacopino, V. A. Marker, R. Triplett, and R. D. Woody, "Implant Materials, Design, and Surface Topographies: Their Effect on Osseointegration. A Literature Review", *The International Journal of Oral & Maxillofacial Implants*, Vol. 15, pp. 675-690, 2000.

6. Rosa, A. L., M. M. Beloti, P. T. Oliviera, and R. Van Noort, " Osseointegration and osseoconductivity of Hydroxyapatite of Different Microporosities", *Journal of Materials Science: Materials in Medicine*, Vol. 13, pp. 1071-1075, 2002.

7. Daculsi, G., O. Laboux, O. Malard, and P. Weiss, "Current State of the Art of Biphasic Calcium Phosphate Bioceramics", *Journal of Materials Science: Materials in Medicine*, Vol. 14, pp. 195-200, 2003.

8. Bagambisa, F. B., U. Joos, and W. Schilli, "Mechanisms and Structure of the Bond between Bone and Hydroxyapatite Ceramics, *Journal of Biomedical Materials Research*, Vol. 27, 1047-1055, 1993.

9. Fulmer, M. T., I. C. Ison, C. R. Hankermayer, B. R. Constanz, and J. Ross, "Measurements of the Solubilities and Dissolution Rates of Several Hydroxyapatites", *Biomaterials*, Vol. 23, pp. 751-755, 2002.

10. Tas, A. C., "Participation of Calcium Phosphate Bone Substitutes in the Bone Remodelling Process: Influence of Materials Chemistry and Porosity", *8th Conference of the European Ceramic Society*, 2003.

11. Murugan, R., K. Panduranga Rao, and T. S. Sampath Kumar, "Heat-Deproteinated Xenogeneic Bone from Slaughterhouse Waste: Physico-Chemical Properties", *Bulletin of. Materials. Science.*, Vol. 26, No. 5, pp. 523–528, August 2003.

12. Mittelmeier, H., B. Mittelmeier, and B. Leu, "*Bone Substitute Material on the Basis of Natural Bones*", US Patent, 4,654,464, 1987.

13. Bauer, G. and F. Vizethum, "*Process or Producing a Bone Replacement Material*", US Patent, 5,133,756, 1992.

14. Johnson, G. S., M. R. Mucalo, M. A. Lorier, U. Gieland, and H. Mucha, "The Processing and Characterization of Animal-Derived Bone to Yield Materials with Biomedical Applications. Part II: Milled Bone Powders, Reprecipitated Hydroxyapatite and the Potential Uses of These Materials", *Journal of Materials Science: Materials in Medicine*, Vol. 11, pp. 725-741, 2000.

15. Anderson, L. A., M. R. Mucalo, G. S. Johnson, and M. A. Lorier, "The Processing and Characterization of Animal-Derived Bone to Yield Materials with Biomedical Applications. Part III: Material and Mechanical Properties of

Fresh and Processed Bovine Cancellous Bone", *Journal of Materials Science: Materials in Medicine*, Vol. 11, pp. 743-749, 2000.

16. Joshi, S. V., M. P. Srivastava, A. Pal, and S. Pal, "Plasma Spraying of Biologically Derived Hydroxyapatite on Implantable Materials", *Journal of Materials Science: Materials in Medicine*, Vol. 4, pp. 251-255, 1993.

17. Oktar, F. N., *Characterization of Processed Tooth Hydroxyapatite and Bioglass for Potential Applications in Dentistry*, Ph.D. Thesis in Biomedical Engineering, Boğaziçi University, 1999.

18. Gokbayrak, H., *Production of Hydroxyapatite Ceramics*, M.Sc. Thesis in Mechanical Engineering, Boğaziçi University, 1996.

19. Goren, S, *Production of Hydroxylapatite from Animal Bone*, M.Sc. Thesis in Biomedical Engineering, Boğaziçi University, 2003.

20. Sivakumar, M., T. S. Sampath Kumar, K.L. Shanta, and K. Panduranga Rao, "Development of Hydroxyapatite Derived from Indian Coral," *Biomaterials*, Vol. 17, pp. 1709-1714, 1996.

21. Narasaraju, T. S. B., and D. E. Phebe, "Review: Some Physicochemical Aspects of Hydroxylapatite", *Journal of Materials Science*, Vol. 31, pp. 1-21, 1996.

22. Richerson, D.W., *Modern Ceramic Engineering*, Marcel Dekker Inc., New York, 1992, 2nd Edition.

23. Reed, J. S., *Introduction to the Principles of Ceramic Processing*, John Wiley & Sons, New York, 1988.

24. Juang, H. J., and M. H. Hon, "Effect of Calcination on Sintering of Hydroxyapatite", *Biomaterials*, Vol. 17, pp. 2059-2064, 1996.

25. Patel, N., I. R. Gibson, S. Ke, S. M. Best, and W. Bonfield, "Calcining Influence on the Powder Properties of Hydroxyapatite, *Journal of Materials Science: Materials in Medicine*, Vol. 12, pp. 181-188, 2001.

26. Fanovich, M. A., and J. M. Porto Lopez, " Influence of Temperature and Additives on the Microstructure and Sintering Behaviour of Hydroxyapatites with Different Ca/P Ratios", Journal *of Materials Science: Materials in Medicine*, Vol. 9, pp. 53-60, 1998.

27. Raynaud, S., E. Champion, and D. Bernache-Assollant, "Calcium Phosphate Apatites with Variable Ca/P Atomic Ratio II. Calcination and Sintering", *Biomaterials*, Vol. 23, pp. 1073-1080, 2002.

28. Zhao, L., J. Zwick, and E. Lugscheider, "The Influence of Milling Parameters on the Properties of the Milled Powders and the Resultant Coatings", *Surface and Coatings Technology*, Vol. 168, pp. 179–185, 2003.

29. Bingon, A., J. Chevalier, and G. Fantozzi, "Effect of Ball Milling on the Processing of Bone Substitutes with Calcium Phosphate Powders", *Journal of Biomedical Materials Research*, Vol. 63, pp. 619–626, 2002

30. Rodriguez-Lorenzo, L. M., M. Vallet-Regi, and J. M. F. Ferreira, "Fabrication of Porous Hydroxyapatite Bodies by a New Direct Consolidation Method: Starch Consolidation", *Journal of Biomedical Materials Research*, Vol. 60, pp. 232-240, 2002.

31. Rodriguez-Lorenzo, L. M., M. Vallet-Regi and J. M. F. Ferreira, "Colloidal Processing of Hydroxyapatite", *Biomaterials*, Vol. 22, pp. 1847-1852, 2001.

32. Tas, C., F. Korkusuz, M. Timucin, and N. Akkas, "An Investigation of the Chemical Synthesis and High-Temperature Sintering Behaviour of Calcium Hydroxyapatite (HA) and Tricalcium Phosphate (TCP) Bioceramics", *Journal of Materials Science: Materials in Medicine*, Vol. 8, pp. 91-96, 1997.

33. Gibson, I. R., S. Ke, S. M. Best, and W. Bonfield, "Effect of Powder Characteristics on the Sinterability oh Hydroxyapatite Powders", *Journal of Materials Science: Materials in Medicine*, Vol. 12, pp. 163-171, 2001.

34. de Groot, K., *Bioceramics of Calcium Phosphate*, CRC Press, Florida, 1983.

35. Jinawath, S., and P. Sujaridworakun, " Fabrication of Porous Calcium Phosphates", *Materials Science and Engineering*, Vol. 22, pp.. 41-46, 2002.

36. Tancred, D. C., A. J. Carr, and B. A. O. Mccormack, "The Sintering and Mechanical Behavior of Hydroxyapatite with Bioglass Additions", *Journal of Materials Science: Materials in Medicine*, Vol. 12, pp. 81-93, 2001.

37. Kalita, S.J., S. Bose, H. L., Hosick, and A. Bandyopadhyay, "CaO–P2O5–Na2O-Based Sintering Additives for Hydroxyapatite (HAp) Ceramics", *Biomaterials*, Vol. 25, pp. 2331–2339, 2004.

38. Vaz, L. A. B. Lopes, and M. Almedia, "Porosity Control of Hydroxyapatite Implants", *Journal of Materials Science: Materials in Medicine*, Vol. 10, pp. 239-242, 1999.

39. Ruys, A. J., M. Wei, C. C. Sorrell, M. R. Dickson, A. Brandwood, and B. K. Milthorpe, "Sintering Effects on the Strength of Hydroxyapatite", *Biomaterials*, Vol. 16, pp. 409-415, 1995.

40. Liao, C. J., F. H. Lin, K. S. Chen, and J. S. Sun, "Thermal Decomposition and Reconstition of Hydroxyapatite in Air Atmosphere", *Biomaterials*, Vol. 20, pp. 1807-1813, 1999.

41. Kim, Y. S., Y. H. Kang, and J. B. Park, "Effect of Bone Mineral Particles on the Porosity of Bone Cement", Bio-*Medical Materials and Engineering*, Vol. 4, No. 1, pp. 37-46, 1994.

42. Baah, C., and J. I. Baah, "Polypropylene Degredation in NaOH Environments", *Materials and Design*, Vol. 23, pp. 341-343, 2002.

43. Onay, A. S., Production *of Ni-Zn Ferrite Transformer Cores*, M.Sc. Thesis, Boğaziçi University, 2002.

44. Rhee, S. H. "Synthesis of Hydroxyapatite via Mechanochemical Treatment", *Biomaterials*, Vol. 23, pp. 1147-1152, 2002.

45. Jinawath, S., D. Pongkao, W. Suchanek, and M. Yoshimura, "Hydrothermal Synthesis of Monetite and Hydroxyapatite from Monocalcium Phosphate Monohydrate", *International Journal of Inorganic Materials*, Vol. 3, pp. 997-1001, 2001.

46. McLean, F. C., and A. M. Budy, *Radiation, Isotopes and Bone*, Academic Press, New York, 1964.

47. Fung, Y. C., *Biomechanics: Motion, Flow, Stress, and Growth*, Springer Verlag, New York, 1990.

48. Fung, Y. C., *Biomechanics: Mechanical Properties of Living Tissues*, Springer Verlag, New York, 1981.

49. Marieb, E. N., *Human Anatomy & Physiology*, Benjamin Cummings, San Francisco, 2001.

REFERENCES NOT CITED

Park, J. B., *Biomaterials Science and Engineering*, John Wiley & Sons, New York, 1984.

Vincenzini, P. (Editor), *Materials in Clinical Applications*, Techna Srl, Italy, 1995.

Pizzoferrato, A., P. G. Marchetti, A. Ravaglioli, and A. J. C., Lee, *Biomaterials and Clinical Applications*, Elsevier Science Publishers, The Netherlands, 1986.

Ohgushi, H., M. Okumura, T. Yoshikawa, K. Inoue, N. Senpuku, S. Tamai, and E. C.,Shors, "Bone Formation Process in Porous Calcium Carbonate and Hydroxyapatite, *Journal of Biomedical Materials Research*, Vol. 26, pp. 885-895, 1992.

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