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Titanium compacts produced by the pulvimetallurgical hydride–dehydride method for biomedical applications

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Abstract
Titanium powder production by the hydride–dehydride method has been developed as a non-expensive process. In this work, commercially pure grade two Ti specimens were hydrogenated. The hydrided material was milled in a planetary mill. The hydrided titanium powder was dehydrided and then sieved to obtain a particle size between 37 and 125 μm in order to compare it with a commercial powder produced by chemical reduction with a particle size lower than 150 μm. Cylindrical green compacts were obtained by uniaxial pressing of the powders at 343 MPa and sintering in vacuum. The powders and the density of sintered compacts were characterized, the oxygen content was measured and *in vivo* tests were performed in the tibia bones of Wistar rats in order to evaluate their biocompatibility. No differences were observed between the materials which were produced either with powders obtained by the hydride–dehydride method or with commercial powders produced by chemical reduction regarding modifications in compactation, sintering and biological behaviour.

1. Introduction

Titanium and titanium alloys have become the preferred materials for many chemical, energy, surgical and aerospace applications because of their unique combinations of low density, good mechanical properties, excellent corrosion resistance and biocompatibility. Despite these attractive features, the use of titanium components is limited by cost [1].

The production of titanium parts by powder metallurgy is one of the tendencies of modern metallurgy, since structures with complex geometries and controlled porosity can be easily obtained [2]. Titanium powder can be used in human medical products such as pacemakers, heart valves, reconstruction devices, skull shells, dental implants and maxillofacial applications [3].

Near net-shape technologies are seen as a major means of reducing the manufacturing costs of titanium alloy components. These processes include powder metallurgy. In these technologies, titanium alloy powders are produced by different processes: rotating electrode, plasma rotating electrode, and hydride–dehydride (HDH), among the most common procedures. Powders produced by the two former processes have spherical particles and high purity, but the production costs are rather high. The powder obtained by the HDH process has an angular morphology, and fine particles are also easily obtained. These are desirable characteristics for sintering, because of their high specific surface area, the driving force for bonding in the sintering process. On the other hand, powders with spherical particles have the poorest

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Table 1. Quantitative analysis of impurities in the material (wt%).

N (max.)	C (max.)	H (max.)	Fe (max.)	O (max.)
0.03	0.08	0.015	0.30	0.25

compacting properties because they provide no mechanical interlocking and have the smallest possible number of contact points. Conversely, the HDH method has a potential for high production volume at relatively low costs [1, 4–6].

The HDH process is applicable to titanium as this metal absorbs large amounts of hydrogen at high temperatures. Room-temperature solubility of hydrogen in this metal is quite low. During the process, brittle hydrides are formed which can be easily milled at room temperature. Heating of this hydrided powder in high vacuum allows hydrogen desorption producing the metallic powder [7, 8].

There are various processes of consolidation and densification of the powders, hot isostatic pressing being the most common procedure. Through the simultaneous application of temperature and pressure, full density in the part is attained by transmission of the applied pressure [4]. Cold pressing to the desired shape and sintering can provide articles at lower cost than hot isostatic pressing. However, cold pressing leads to structures with some porosity, thus reducing the mechanical properties of the components [6]. Therefore, it is useful when the component will not be subjected to extreme conditions. Thus, the evaluation of the material biological properties is a *sine qua non* need. It must be guaranteed that materials have no deleterious effect in contact with tissues before they are marketed and used routinely in the clinic [9, 10].

The final purpose of this line of work is to produce biocompatible Ti base powder alloys with different porosity levels using a low cost method. Hopefully, a powder of a quality adequate for medical applications from implants (bulk pieces or coatings) to metallic scaffold will be produced. In this previous stage, the study was focused on the analysis of compactation, sintering and porosity levels of the powders produced by HDH in our laboratory. The performance results were compared with commercial powders produced by chemical reduction. For this purpose, a comparative study of biocompatibility of both powders was also made in Wistar rats' tibia bones.

2. Experimental procedure

2.1. Material

The material used in this study was received as 2 mm thick, rolled and recrystallized titanium grade 2 strip. The main impurities are shown in table 1.

Prior to hydrogen charging, samples of dimensions $40 \times 12 \times 2\,\text{mm}^3$ were cut and mechanically polished. The specimen surface was successively cleaned with trichlorethylene and ethyl alcohol.

The hydriding process was performed in a Sieverts' apparatus (figure 1). It consists of a quartz tube (25 mm diameter and 500 mm length) where the samples to be charged are introduced, one end of the tube being closed and the other end connected to a vacuum and gas input systems. The heat treatments were performed by sliding an instrumented furnace on the hydrogenation chamber. Temperature was measured by means of a thermocouple installed in the chamber.

Hydriding was done at 600 °C and pressures close to 0.1 MPa until the hydrogen concentration in the samples was 1.5 H/Ti. Hydrogen concentrations in the specimens were calculated by two methods: (1) by evaluating the difference between the initial and final pressures assuming ideal gas behaviour and (2) by weighing the samples before and after hydrogenation in a precision balance with an error of 10^{-5} g.

The hydrided samples were milled, under vacuum, with a Retsch Planetary ball mill PM400 model using stainless steel receptacles and 20 mm diameter balls.

The milling speed in the planetary mill was 200 rpm and the milling time was 10 min. The obtained powder was separated via mechanical sieving in a vibrating sieve with aperture sizes of 37, 74, 125 and 400 μm.

The dehydriding of the titanium powder was carried out in the Sieverts' apparatus at 600 °C in dynamic vacuum conditions. The powder was put in a stainless steel capsule during dehydriding to avoid being absorbed by the primary rotary pump in the former pumping stages. After dehydriding, high purity argon was injected into the quartz tube up to room atmosphere in order to prevent powder ignition. Finally, the argon was gradually replaced with air. During dehydration, the powder was partially sintered, and then it had to be milled and sieved again.

Uniaxial cold pressing was carried out at 343 MPa, without a binder, in order to obtain cylindrical green compacts (diameter 8 mm and length 10 mm). The green compacts were sintered at 1300 °C for 2 h under a dynamic high vacuum of 10^{-5} Torr in the apparatus shown in figure 1. Two kinds of samples were obtained: HDHS (samples prepared using hydride–dehydride powders) and CPS (samples prepared with commercial powders).

The oxygen incorporated in the samples throughout the process was measured by the vacuum–fusion method.

The densities of the sintered compacts were determined by the Archimedes method.

2.2. Animal model

Twelve male Wistar rats (300–350 g) were included in this study. The animals were housed at controlled temperature and light–dark cycles of 12 h with *ad libitum* access to food and water.

The rats were handled and maintained in accordance with international recommendations [11].

2.3. Implant surgery

All surgery was performed under sterile conditions. General anaesthesia was obtained by intraperitoneal administration of ketamine chlorhydrate (14 mg kg^{-1}) and acepromazine (10 mg kg^{-1}). The rats' legs were clipped of all hair, prepared with a povidone–iodine solution and draped for surgery. A longitudinal skin incision was made in order to expose the tibial

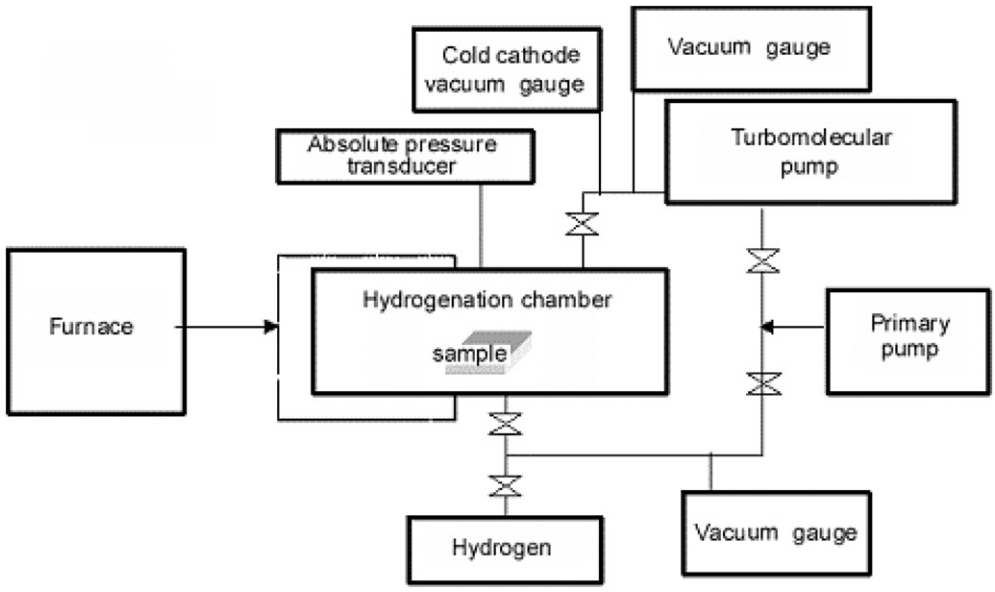

Figure 1. Sketch of the Sieverts' apparatus.

crest in both legs. After incising and raising the periosteum, a cortical window was excised with a hollow drill with sterile saline irrigation. In the right leg, a cylindrical Ti implant (1.6 × 2 mm) was placed inside the bone and the wounds were closed in layers with silk. In the left leg, a similar procedure was performed in order to place a cylinder (1.6 × 2 mm) of HDHS or CPS, depending on the study group. This procedure resulted in six rats carrying Ti and HDHS implants and another six animals with Ti and CPS implants. Neither antibiotics nor anti-inflammatory or analgesic therapy was employed. The rats were carefully supervised in the post-surgical period for complications including pain, discomfort or infection. Animal health was also monitored through changes in body weight.

Healing periods of 14 days and 60 days were allowed for half of the implants, respectively. After 14 days and 60 days, the animals were killed (six rats each) with an intravenous anaesthetic overdose. Following euthanasia, the tibiae were removed and fixed in 10% buffered formol for 48 h. Undecalcified sections were embedded in methacrylate resin, ground and polished, and finally stained with aniline blue.

The specimens were blindly evaluated by two independent observers using a light microscope coupled with a digital camera Canon Powershot A510 in order to study the bone-to-contact areas.

3. Results and discussion

3.1. Material

When selecting a biomaterial for implantation in bone, biocompatibility and osseointegration are two of the most desirable properties. For this purpose, various types of implant materials are currently investigated in an attempt to find one that presents greater efficiency and reduced time for bone repair. In the present experiment, compacts have been fabricated from titanium powder produced by the HDH method and compared for biocompatibility with compacts made from the commercial powders pressed and sintered in similar conditions. To obtain HDHS, Ti grade 2 was hydrided to get a hydrogen concentration of 1.5 H/Ti. In this condition, titanium transforms completely into titanium hydride and the embrittlement level allows rapid milling. This point was considered important in order to avoid powder oxidation and minimize Fe contamination. A material with lower hydrogen content requires longer milling times. The hydride powder thus milled was separated by particle size by sieving for 30 min (table 2).

Table 2. Particle size distribution of the titanium hydride powder.

Particle size	Mass fraction
>420 μm	0.12
125–420 μm	0.26
74–125 μm	0.17
37–74 μm	0.25
<37 μm	0.20

Figure 2 shows the typical angular morphology of hydride powder obtained by the HDH method.

The dehydriding stage was carried out by heating the powder up to 700 °C. During the desorption process, the temperature was gradually increased holding a pressure of 10^{-4} Torr. The obtained powder was metallic grey and, in some cases, partially sintered (indicating the high sinter reactivity of the powder) as shown in figure 3. It was then necessary to mill and sieve it again, in order to obtain dehydrided Ti powders.

Figure 4 shows the metallic powders obtained by HDH and the commercial powder.

Cylindrical cross-section green compacts were produced by uniaxial cold pressing of the titanium powders with particle sizes between 37 and 125 μm.

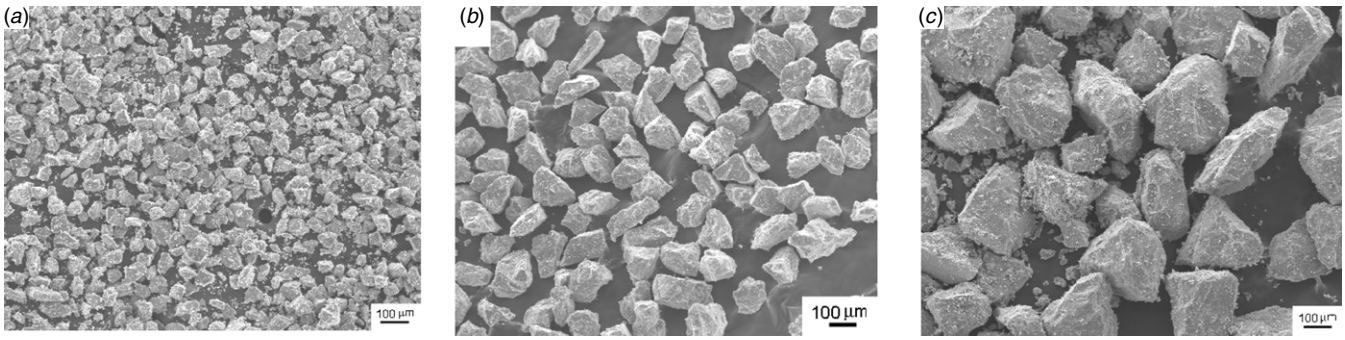

Figure 2. Hydrided powder produced in our laboratory with particle sizes between (*a*) 37 and 74 μm; (*b*) 74 and 125 μm; (*c*) more than 125 μm.

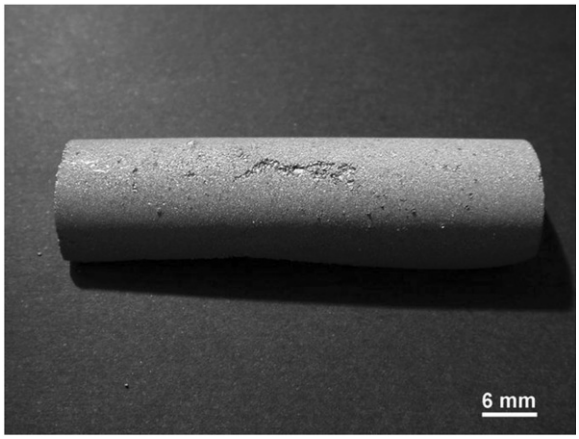

Figure 3. Dehydrided titanium powder slightly sintered during the dehydriding process.

Figure 5 shows the porosity of materials obtained after sintering the green compacts from powders obtained in our laboratory (figure 5(*a*)) and from a commercial powder (figure 5(*b*)).

The density of the green compacts and the sintered materials is shown in table 3. As can be seen, no relevant differences were found in sintered materials from both types of powders.

Table 3. Relative density (expressed in % of the theoretical density).

Powder	Green preform density	Compact density
Commercial	71.1	85.0
HDH	64.0	87.4

On the other hand, the compacting and sintering behaviour between the hydride–dehydride powder and the commercial powder produced by chemical reduction was similar to that reported in 1961 by Schwope [12] under the same conditions of pressure and temperature. Schaefler *et al* [2] reported that a titanium structure with complex geometry and controlled porosity was relatively easy to obtain when using some metallurgy strategies. In this respect, our results agreed with those of others [1, 4–6] and seem promising with respect to the use of a low-cost method (HDH) of producing Ti powder.

In the sintered HDHS compact, the oxygen content was found to be lower than 5000 ppm and in the CPS compact it was lower than 2000 ppm. Titanium is a highly reactive metal that readily passivates to form a protective oxide layer (approximately 10 nm thick). This reactive nature of titanium can be seen both as an advantage and a disadvantage for its use: as the protective oxide layer provides a highly biocompatible surface and a corrosion resistance similar to that of noble metals, but contamination with even low concentrations of

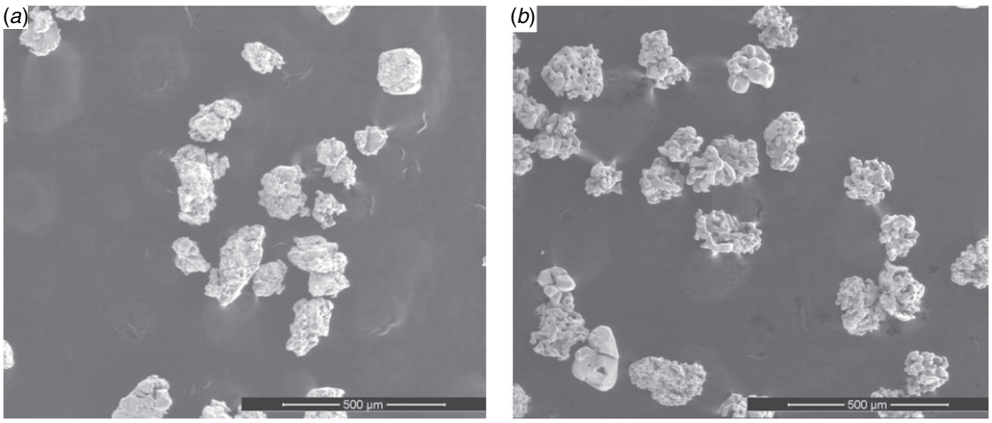

Figure 4. Metallic powder obtained by: (*a*) HDH; (*b*) metallic commercial powder.

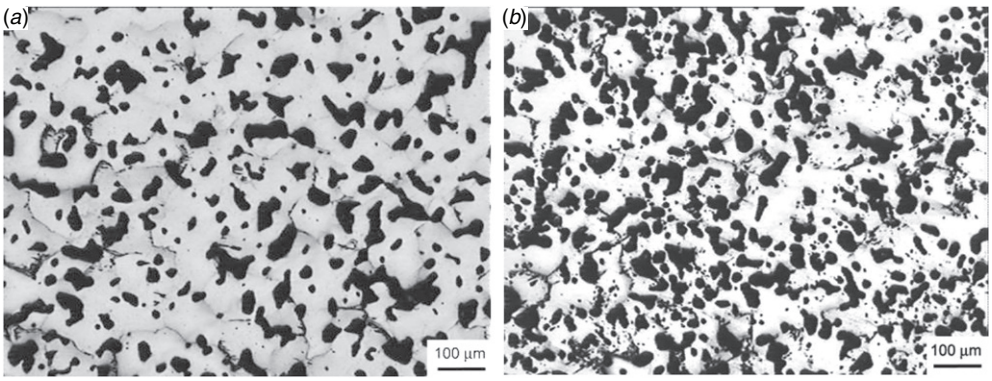

Figure 5. Optical image of the compacts pressed at 343 MPa and sintered at 1300 °C for 2 h: (*a*) sintered compact from powder produced in our laboratory (HDHS); (*b*) sintered compact of the commercial powder used as a reference (CPS).

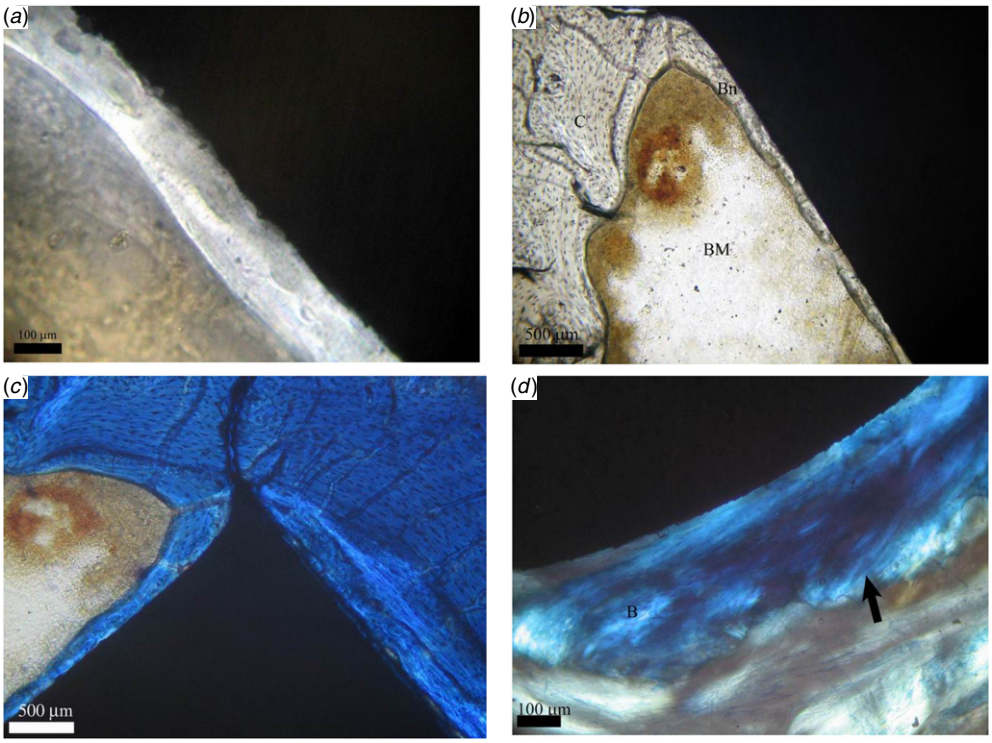

Figure 6. Microphotographs of three materials at 60 days postimplantation: (*a*) bone–Ti interface viewed by transmitted polarized light microscopy (unstained). Note the bone in close contact with the Ti implant; (*b*) the bone from the cortical (old bone) (C) is observed making contact with the HDHS implant (black). Bn = neoformed bone; BM = bone marrow (unstained); (*c*) Ditto B stained with aniline blue (HDHS). (*d*) Bone (B) in close contact with the CPS implant observed by polarized light, stained with aniline blue. Note the fibrilar structure (arrow).

(This figure is in colour only in the electronic version)

atmospheric oxygen can lead to a significant loss of ductility [13].

3.2. Clinical observation

During the experimental periods, the rats were carefully supervised for complications including pain, discomfort, signs of infection and changes in body weight. All animals remained in good health throughout the study. At the end of the experiment, the rate of animal survival was 100%. The animals recovered well after surgery without signs of stress at the time of harvest. The possible minimal differences in the vital signs that can be objectively measured and observed among animals did not reach clinically significant levels. Visual macroscopic observation revealed that the implants could be easily located while all of them remained *in situ* and anchored monocortically.

3.3. Histological analysis

In this study, a rat tibia model was used with the main objective to microscopically analyse the behaviour of the bone tissues

to the tested HDHS and CPS materials. This model was based on a previously described one for studying the performance of different types of biomaterials [14] allowing to mimic a clinical situation in which an implant material was inserted into the bone. Similar success rates were obtained in the human implant situation, and the rat tibia established the reliability of this method for the placement of implants [15]. The advantage of this model is the possibility of investigating bone formation in the gap and bone ingrowth in the implant under very controlled circumstances. The bone healing is not affected by weight loading and takes place in a purely osseous environment. A disadvantage is the lack of similarity to the clinical situation where such controlled situations are not found [16].

Implant placement in bone is presently associated with defined expectations of success which has been correlated to the histologically represented bone–implant interface and is commonly referred to as 'osseointegration' [17].

Light microscopic observation showed that all implants have an uneventful healing with a normal pattern of bone repair and without signs of immunologic and inflammatory reactions. In all instances, direct bone-to-implant contact could be achieved during the observation periods. Histological analysis of the bone/implant interface revealed an intimate contact between the titanium surface and the bony implantation bed in all groups allowing for a progressive integration of the materials into the bone.

On day 14, in the three groups, fibrillar structures in close contact with metal in focalized areas were detected by polarized light. These structures were collagen fibres and immature bone.

On day 60, in all groups, mature bone was observed in close contact with metal in wide areas (figure 6). The bony apposition revealed a laminar structure containing individual osteocytes and haversian canals (figures 6(*b*) and (*c*)). In accordance with our results, other authors [18, 19] demonstrated that immature woven bone first appeared around titanium implants and was replaced by mature lamellar bone by 56 days after implantation in rats, suggesting that osseointegration was almost complete at this time.

4. Conclusions

Compacts have been fabricated from titanium powder produced by the HDH method and compared with compacts made from commercial powders pressed and sintered under similar conditions. Main results are as follows.

(1) No differences were observed in compactation and sintering behaviour between the HDH powder and the commercial powder produced by chemical reduction. The density of the compacts obtained from powders produced in our laboratory is similar to that of the compacts from commercial powders.

(2) Oxygen contamination must be lowered in the powder produced in our laboratory in order to avoid possible loss of ductility.

(3) The above results of *in vivo* tests support the conclusion that HDH processing of titanium has not introduced any negative feature as regards biocompatibility and produces a similar biological response to commercial titanium obtained by other processing methods.

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