The Study of Controlled Relaese of Indomethacin Drug From Prepared Apatite Compounds Containing The Elemantal Calcium And Strontium

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Abstract— Apatite compounds has wide applications in the medical and non-medical field and are very stable compounds .Different compounds of apatite were prepared and identified such as a that of calcium hydroxyapatite, Strontium Fluorapatite compound and Strontium –Calcium hydroxyapatite compound . All these compounds were identified by Infrared spectroscopy and X-rays, which confirmed the presence of the prepared compounds. The release of a indomethacin drug in a laboratory in the prepared compounds were studied. Porosity tablets of the compounds were prepared using the material (Micro Crystalline Cellulose) as a porous. then removed the used cellulose material as a porous by heating in oven at 600 C° for two hours. These tablets was examined using scanning electronic microscope (SEM) which shows the presence of different porous sizes in the prepared tablets .

keywords — Apatite ,drug delivery , hydroxyapatite , flourapatite , x-ray , micro crystalline cellulose , SEM, .

1 INTRODUCTION

They mineral apatite in bones , teeth , sedimentary rocks , igneous and metamorphic rocks. They have many colors such as :(green, blue, yellow, white, red, pink, brown and colorless [1] .The apatite compounds are thermally very stable which attract the attention of many scientists and researchers due to its composition which has the ability to resist high temperatures [2,3] .

Hydroxyapatite (HAP) is the inorganic compound of calcium phosphate which is made of ceramic materials, biological compounds

Group, and is a metal component President in bones , teeth ,rocks and in the sea coral [4,5] . Hydroxyapatite is a crystalline substance which is organized hexagonal crystals binary system engineering pyramid .The molecular formula is: Ca10 (PO4) 6 (OH) 2 .

The term apatite can be described in general formula: M10 (XO4) 6Z2 , as M represents a metal which may be (Ca2 +, Ba2 +, Sr2 +, Pb2 +, Mg2 +, Zn2 +, Si2 + or Na +), and X represents the (P5 +, V5 + or Mn5 +), while Z represents the ions (Cl-, F- or OH-) [6] .

Hydroxyapatite attract the attention of researchers in the field of biomedical applications due to its great similarity in the composition and structure between teeth and bones. It has the ability to absorb some of the organic compounds and therefore has been used widely as agents of separation of proteins and amino acids in resins Chromatography column. Also used as additives in toothpaste, and in the gas sensor components in ionic conductors, and medically as Osteoimplants [7,8] .

Hydroxyapatite active ingredient Bioactive biology and material of harmony vital and biological Biocompatibility so coated by some of the parts that are grown in the body, such as parts made of titanium and stainless steel , Other characteristics of hydroxyapatite which makes material have a vital agree that it does not dissolve in the body of the object neighborhood due to very high melting point "up to 1250° "

In recent years several types of composite materials (polymer-hydroxyapatite) as materials to replace the bone are developed. The purpose of the integration of the polymer with HAP is to support and improve the properties of bonding with the bone. It has been found that the HAP in such compound have around from the polymer material is biologically active "compound linked to the bone with the same time and can improve the mechanical properties, especially the flexibility and hardness coefficient Elastic Modulus and Hardness [9,10] , The HAP's complex structure has advantage of adding a good absorbance of various pharmaceutical products such as antibiotics, hormones and steroids. Used as a composite HAP with antibiotics HAP-Antibiotics and successfully used for the launch of slow pharmaceutical compounds [11-13], has proved of medication received good efficiency in the treatment of diseases such as system, Bone infections Osteomyelitis and osteoporosis (osteoporosis) Osteoporosis and bone cancer Osseous Cancer [14] .

The aim of these paper to develop some composite of HAP with indomethacin as slow release device . .

1.1 EXPERIMENTAL

A) Preparation of Strontium Flourapatite

A solution 100 ml containing (4.356 g) of di ammonium hydrogen phosphate and (1.152 g) of ammonium fluoride are mixed and heated to the boiling point at (pH = 9) by adding ammonium hydroxide solution and then added strontium nitrate solution (8.295 g) slowly to the hot solution with vigorously stirring for 3 hours and then filtered by Vacuum Filtration and wash with distilled water. The sediment placed in the drying desiccator at room temperature for 12 hours before grinding to a powder. The powder heated at a temperature of 150 C ° for two hours and then at a temperature of calcined at 1000 C ° for two hours [15,16] .

B) Preparation of Calcium-Strontium Hydroxyapatite

A solution 500ml contain (0.25 mol) of calcium nitrate tetra hydrate and (0.25 mol) of strontium chloride hydrate , and the solution 500 ml of Di ammonium hydrogen phosphate (0.3 mol), are placed in flask and heated to 80 C ° for 3 h at (pH = 10) by adding ammonium hydroxide solution, Then the solution washed several times with distilled water and then rinse with ethanol, dried filtrate at 100 C ° for one hour one and placed at 1000 C ° for two hours [17] .

C) Preparation of Hydroxyapatite Powder Using Sol-Gel Compound

Phosphoric acid solution (0.25 M) (pH = 10) was added with stirring to calcium nitrate tetra hydrate solution (1 M) very slowly while maintaining (pH = 10) by adding ammonium hydroxide solution. The solution is shaken vigorously for one hour and left at room temperature for 24 hours, then dried at 65 C ° for 24 hours and washed with water several times to get rid of nitrate and ammonium ions and heated to 1000 C ° for two hours [18] .

D) Preparation of porous tablets of prepared compounds

Powder material (Microcrystalline cellulose) was mixed with prepared compounds by ratio (25% w / w) to get the porous. Samples compressed tablets on the weight of each tablet form (0.5 gm), then these tablets are exposed to temperature 600 C ° for two hours to get rid of cellulose material and get a clear picture of porous in the scanning electronic microscope device.

1.2 Drug Loading and Release

(0.5 gm) of the drug was used with (0.5 g) of the tablets prepared compounds in (20 ml) of buffer solution at (pH = 7.4) for 24 hours with stirring (shaker).The tablet placed in (10 ml) of buffer solution at (pH = 7.4) and measured absorbance at different times to follow up the release at a wavelength of 320 nm, The absorbance measured at time per 15 minutes in the first two hours, then measurement every 30 minutes in the next five hours, and every four hours for the remaining in 24 hours.

2

2 RESULTS AND DISCUSSIONS

2.1 IDENTIFICATION OF COMPOUNDS BY IR

SPECTROSCOPY

is shown in Figure (1) . The peak appeared at (3440 cm^{-1}), which is back to the group (OH Stretching), and the peak at (1064.63 cm^{-1}) which is back to the group (PO Asymmetric Stretching), while the peak back to the group (PO Symmetric Stretching) is appeared at (1002.92 cm^{-1}), and the peak to (PO Deformation Group) was appeared at (563.18 cm^{-1}) . Figure (2) represent an infrared spectrum of Strontium Flourapatite compound (SrFA), the band belong to (PO Asymmetric Stretching group) appeared at (1078.13 cm^{-1}), while the band belong to (PO Symmetric Stretching Group) is appeared at (1035.77 cm^{-1}) , also the one peak at (592.11 cm -1) is return to (PO Deformation group). The Infrared spectrum of Strontium Calcium hydroxyapatite compound (SrCaHA) is shown in Figure (3). The peak at (3480cm^{-1}) due to the (OH) group , while the band due to (PO Stretching Symmetric Group) was appeared at (1035.70 cm^{-1}) , and the (PO Stretching Asymmetric group) appeared peak at (1108.99 cm^{-1}) also appeared peak back to the (PO Deformation) group at (599.82 cm^{-1}). Table 1 show the main peak in the prepared

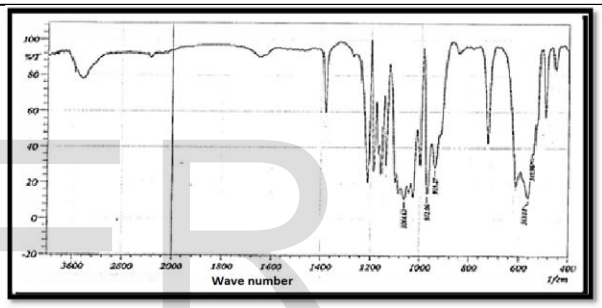

Fig. 1 Infrared spectrum of calcium hydroxyapatite prepared by Sol-Gel

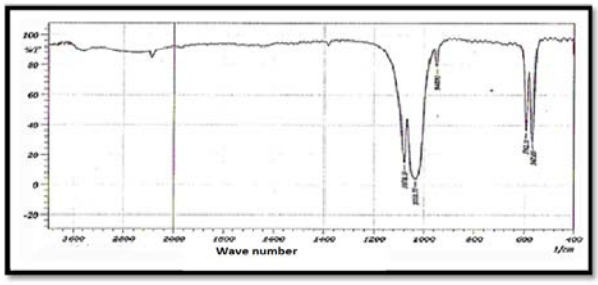

Fig. 2 infrared spectrum of Strontium Flourapatite compound (SrFA)

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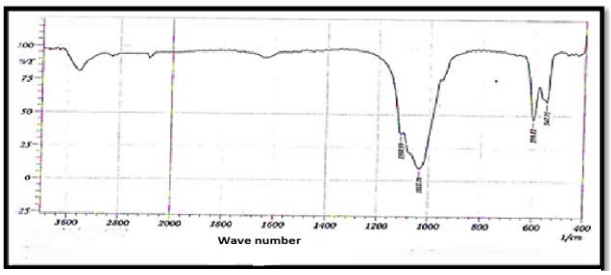


Fig. 3 infrared spectrum of Strontium Calcium hydroxyapatite compound (SrCaHA)

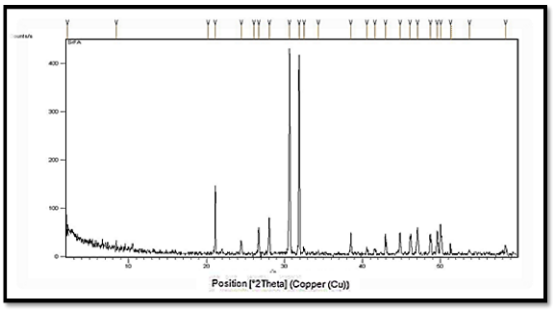


Fig. 5 x-ray diffraction spectrum of SrFA

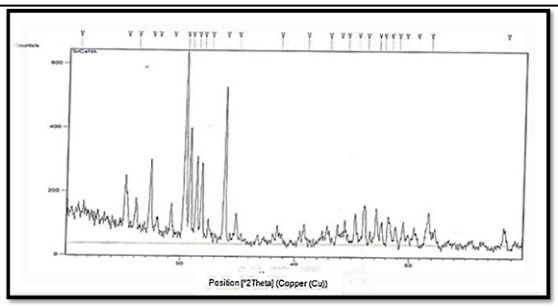


Fig. 6 x-ray diffraction spectrum of CaSrHA

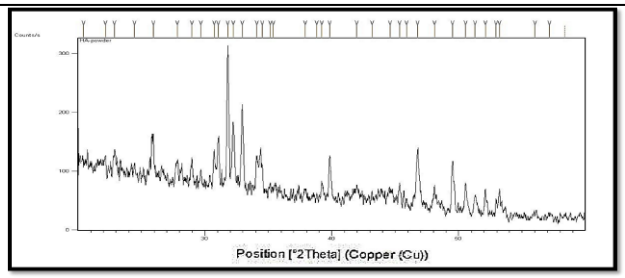
2.2 Identification of Compounds by X-ray Diffraction (XRD)

The X-ray diffraction (XRD) of th
e prepared compounds are shown in figs (4-6) which represents Finger Print for compounds . The most important thing to confirm the installation of the compound is the value of d value , which represents the distance between atomic planes in the crystal [19] . The value of d2θ was calculated according to the equation derived from Barak Bragg Law [20].

d (nm) = 154/2 sin θ

As θ represents the angle between the incident X-ray beam and the levels of the crystal surface.

It showed a very high correspondence with d2θ calculated for apatite compounds and installed the values in the literature (XRD) approved [21] .



. Fig.4 x-ray diffraction spectrum calcium hydroxyapatite prepared by Sol-Gel

3 Quantitative Analysis

Both calcium and phosphate represent the major inorganic components in bones and teeth and hydroxyapatite. Spectral complex of Phosphomolybedenum blue method was used to determine the phosphate concentration in the prepared compounds, at a wavelength of 660 nm [20]. The results were shown in Table (5).

Flame atomic absorption spectrometry was used to measure the elemental concentration of calcium and strontium in the prepared compounds and the results were shown in Table (1)

TABLE 1
the ratio f calcium and strontium in the prepared compounds

compounds	Contraction of phosphate (ppm)	Percentage of calcium %W/W	Percentage of strontium %W/W
Calcium Strontium Hydroxyapatite (CaSrHA)	0.830	18.39	21.72
Strontium Flourapatite (SrFA)	2.250	———	32.27
Calcium Hydroxyapatite powder (CaHAP Powder)	0.867	27.086	———

5 Scanning Electron Microscope

The Scanning Electron Microscope (SEM) gives pictures of the samples by scanning the beam center of electrons with high energy to generate a variety of signals on the surface of solid samples signals that arise from interactions electronic form giving information about the external morphology and chemical composition and crystal structure of the samples , as can the number of times magnification control device (SEM) to about 500,000 visits [22] . The following SEM figures show a picture of the prepared compounds . It is shown the porous in prepared tablets and size of these porous . the figures (7-9) represent images prepared compounds in scanning electron microscope

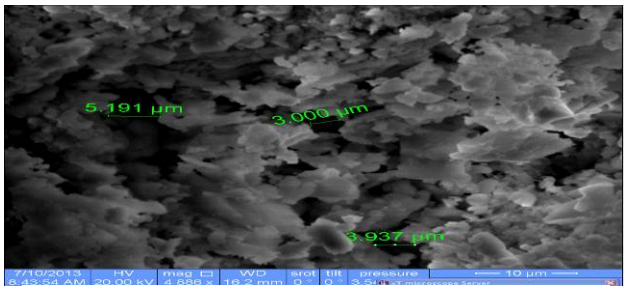


Fig.7 CaHAP powder

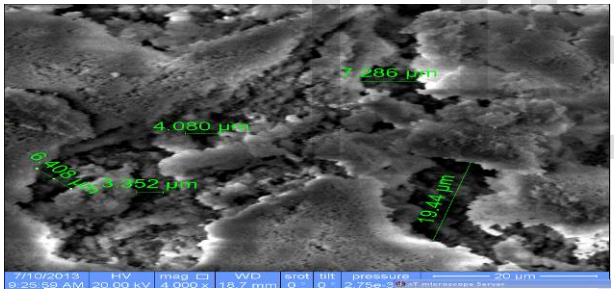


Fig. 8 SrFA

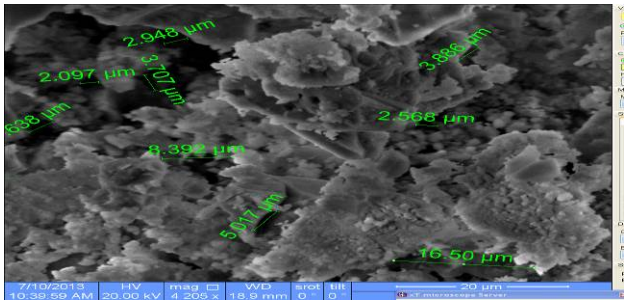


Fig. 9 SrCaHA (mix)

6. The Loading and Release of Drug

The loading and release of the drug was studied under physiological conditions (in vitro), as has been loaded prepared compounds tablets with indomethacin drug, which is used in patients who suffer from arthritis treatment . Prepared porous tablets by mixing Micro Crystalline cellulose material with the prepared compounds by 25%W/W) and through curves were obtained shown that the release mechanism of the drug is by diffusion process, The measured absorbance with time at wavelength 320 nm , show that the release of the drug ratio varies from compound to another.

The release of Strontium flourapatite compound (SrFA), who was the loading percentage (42.50%), which reached release ratio (22.50%) two hours later, after three hours later was (35.46%), , And reached the level at (66.58%) which it stabilized After 8 hours and remained stable at this level even after 24 hours. The compound Strontium Calcium Hydroxyapatite was loading (47.8%), it is found that the release reached (24.63%) after half an hour, after one hour (56.04%) , after two hours and the release percentage was (82.09%) ,and reached the level at (82.44%) which it stabilized After 5 hours and remained stable at this level even after 24 hours. The release in Calcium Hydroxyapatite compound prepared by sol-gel, which was loading (32.8%), the release reached (19.89%) after an hour, two hours after the release reached to (44.35%), after 4 hours reached (78.23%) and reached the level at (78.54%) which it stabilized After 6 hours and remained stable at this level even after 24 hours. (Fig. 10) Shows the release of the drug from prepared compounds.

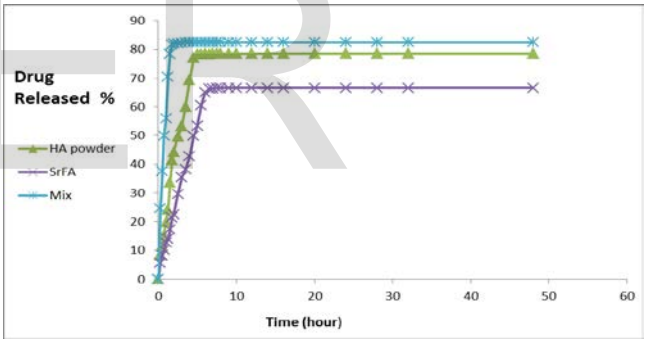


Fig. 10 the release of the drug from prepared compounds.

4 Conclusion

Of the study load and release of the indomethacin drug from apatite prepared compounds showing that the release of the drug with the ratio of release take different time depending on the compounds and measure the percentage of calcium and strontium in the prepared compounds.

In future preparation apatite compounds containing other elements such as barium Ba and silicon Si and Mg magnesium, sodium Na, lead Pb. And replace ions PO4 in CO3 and use of other drugs anti-arthritis is indomethacin .

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