Magnesium-Doped Brucinium Hydroxyapatite: A Versatile Material for Biomedical Applications

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Abstract:

Hydroxyapatite being a biocompaitable material, which closely resembles the mineral phase of bone, it has been used for various biomedical application such as implantation, augmentation and drug delivery etc. Magnesium being a potential trace element towards the enhancement of physiochemical properties of HAP and brucine being an effective traditional medicine extracted from plant alkaloid, together promotes to the effective biomaterial for various applications. A dual dopant: Magnesium and Brucine incorporated with hydroxyapatite nanoparticles (Mg-BHAP) were prepared by a hydrothermal method using calcium nitrate and diammonium phosphate as precursors.The characterization indicates the successful synthesis of Mg-BHAP, demonstrating clamped-shaped morphology and sizes ranging from 80 to 130 nm. FTIR analysis revealed typical absorption bands of hydroxyapatite, while XRD patterns matched known standards for HA, indicating a hexagonal phase. The UV-VIS-NIR optical absorptions study highlights the electronic and structural modification due the dopants confirms the potential application in the field of optical filters and bio-photonics.

Keywords: Hydroxyapatite, dual dopant, trace element, plant alkaloid, FTIR, XRD, SEM, UV, biomedical.

1. Introduction:

Hydroxyapatite (HAP) is a calcium phosphate material with the chemical formula of Ca_{10} $(PO_4)_6$ $(OH)_2$ which has the stoichiometry Ca/Po ratio as 1.67 makes a vital compound in the area of biomedical research for the biocompatible, osteoconductive, chemical stability seamlessly integrate with the tissues, supporting an extensive range of application in regenerative medicine and tissue engineering. HAP yields more attention for the resemblance of mineral compound of human bone & teeth. It employs in the bone grafting, scaffold, implantation coating to encourage osseointegration optimizing the performance and longevity of prosthetics [1]. Also exploited in the field of dental for its dental filler, cement and remineralization therapies owing the potential to adhering with

enamel & dentin.The HAP incorporated toothpaste obtain the honor for microcracks repairment & strengthening of teeth [2]. The pure HAP, itself limits for abilities of physiochemical properties. HAP can be easily integrated with the dopants in its lattice, due to this invaluable ability the recent advances in HAP is customized with the dopantsuitable for corresponding application. The elemental doping for trace and rare earth elements enhances the properties such as mechanical strength, bioactivity, luminescence, antibacterial activity etc., which makes perfect in drug delivery, tissue engineering and bone regeneration applications [3,4]. The Rare Earth dopants is potential upgrades the fluorescence and imaging properties for bioimaging and theronosticsapplication [5]. The trace elements enhance the benefit of antioxidative& osteogenesis properties [6,7].

The Magnesium (Mg), an ideal element plays the vital role in various biomedical applications in regenerative medicine, tissue engineering and drug delivery on biocompatibility, biodegradability, cellular process, bone health, osteogenesis [8]. Notoriously, magnesium- substituted hydroxyapatite enhances the physiochemical properties and bioactivity which promotes toward the bone regeneration and healing [9]. The anti-inflammatory and anti-bacterial corroborate faster recovery and reduces the infection risks during medical implantation [10]. The Mg related materials are potentially examined for facilitating controlled and sustained release of therapeutic agents and improving treatment efficiency for drug delivery system [11].

In research, an alkaloid has been a main ingredient among the 5% of crude drug in treating various diseases, among them 1% was garbed by brucine. The Brucine, a natural plant alkaloid, weakly basic extracted from the matured seeds of strychnosnux-vomica Linn yielded from China, Australia, Burma, Thailand and East India has been mainly used as a Chinese traditional medicine for treating diabetes, anemia, gonorrhea, cancer [12]. Further, it helps to improve the blood circulation and rheumatic and pain relief [13]. Brucine has an unbelievable antitumor activity and plays a potential therapeutic agent for colan cancer in decreasing the tumor weight and volume [14]. With the pharmacological advantages of brucine, it has been substituted with HAP which enhances the bone regeneration, anti-inflammatory effects, controlled drug release in the target. The physiochemical properties of Brucine substituted HAP benefits for the bone healing (bone defects, factures and bone diseases) and drug delivery [15]. In recent study, brucine substitute hydroxyapatite nanoparticles were reported for the optimized brucine concentration, biocompatibility by reducing the toxicity of brucine, which refines the efficiency for the biomedical applications

[16]. The objective is to synthesis the Mg- doped brucinium hydroxyapatite nanoparticle (Mg-BHAP) by hydrothermal method, which may serve as an effective biomaterial in treating various diseases and for biomedical application.

2. Methodology:

2.1 Materials:

Calcium nitrate tetrahydrate ($Ca(NO_3)_2.4H_2O$) (Merck >98.0%) and diammonium hydrogen phosphate $(NH_4)_2\ HPO_4$ were used as precursors, brucine ($C_{23}H_{26}N_2O_4$) (Loba, 99%) and magnesium chloride hexahydrate ($MgCl_2 \cdot 6H_2O$) (Sigma Aldrich, 99.9%) were added as a dual dopant.

2.2 Methods:

Calcium and phosphate were taken in a molar ratio of 1:6. The pH was maintained at 9 by adding liquid ammonium (NH_4OH). The composition of brucine is 1%), while the doping percentage of magnesium chloride hexahydrate was varied at 0.5%, 1%, and 2%. The synthesis was carried out using a hydrothermal method at a temperature of 180°C for 24 hours. Mg-doped brucinium hydroxyapatite nanoparticle was obtained after centrifugation and subsequently dried at 100°C.

2.3 **Characterization techniques:**The synthesized Mg-BHAP were characterized using various techniques are as follows X-ray Diffraction (XRD) (Davinci X-ray diffractometer with Cu Kα (λ = 1.540 Å)), Fourier Transform Infrared Spectroscopy (FTIR) (Thorlabs LM74S2 Driver, Thorlabs Laser Diode Control LDC2000-2A). Scanning Electron Microscopy (SEM) (Carl Zeiss, Model: EVO 18), UV-vis-NIR (UV) (Perkin Elmer Lambda 950, U.S).

3. Characterization of Mg-doped brucinium hydroxyapatite (Mg-BHAP):

3.1 X-ray diffraction:

X-ray Diffraction (XRD) is a non-destructive cornerstone technique applicable for wide range of materials such as metals, ceramic, polymers and biological materials. XRD works on the principle that constructive interference of X-rays is scattered by atomic planes in the crystalline material and it produces the diffraction pattern with respect to the crystal structure of the material. XRD helps in analyzing the structural properties, phase composition, crystallinity, it offers invaluable insights into behavior of materials. The XRD

diffraction pattern of synthesized hydroxyapatite and Mg- doped brucinium hydroxyapatite higher percentage (2%) is shown in the figure (1).

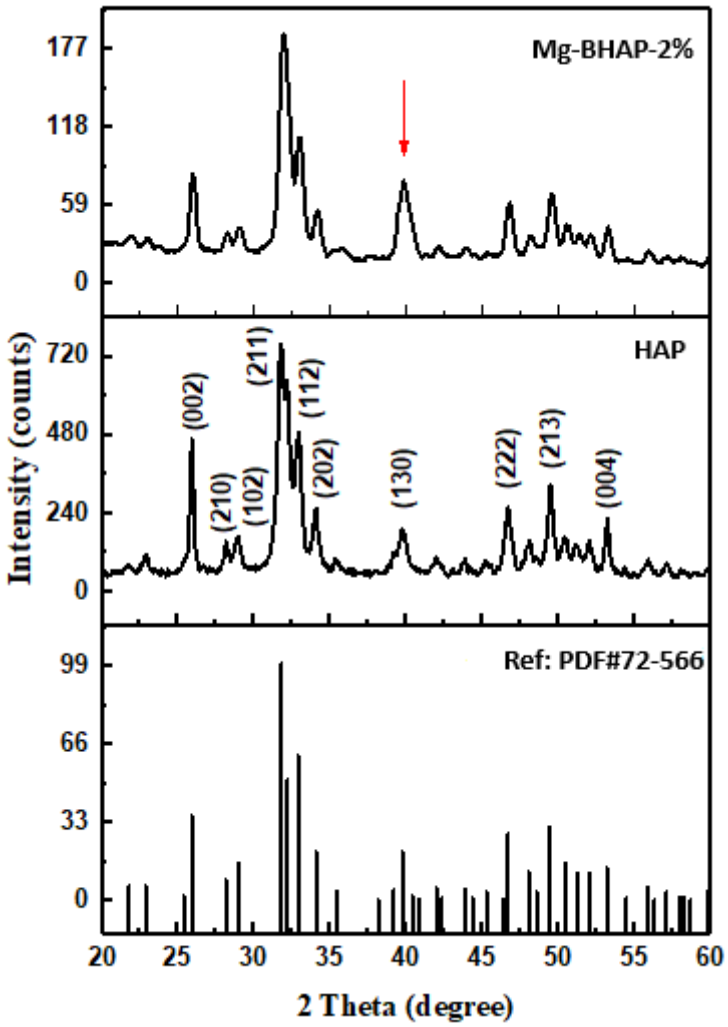

Figure (1) XRD- Hydroxyapatite and Mg- doped brucinium hydroxyapatite 2%

The main phases of synthesized hydroxyapatite well align with the standard diffraction JCPS data (Ref – PDF#72-566), the hexagonal structure of the space group PD3/m with the lattice parameter of a = b = 9.4Å and c = 6.8 Å (Card No: 01.074-0566). The peak at 40°, the intensity increases with increase dopant percentage. Though, the percentage of dopant is minimum the parent structure remains unchanged. Similar changes were reported for incorporation of brucine with hydroxyapatite [16]. The XRD pattern also determines the crystalline size through the Gaussian fit using Full Width at Half Maximum (FWHM).According to the Scherrer equation:

$$Crystalline\ Size(D) = \frac{0.9\lambda}{\beta\ cos\theta}$$

where λ = 1.5405 Å (wavelength of Cu-Kα radiation), β is the FWHM of the peaks, and θ is the Bragg diffraction angle. With the Scherrer equation, the crystalline size of synthesised Mg-BHAP 2% were found to be around 80 to 117 nm. The similar crystalline size of HAP was observed with the previous researcher for various biological application. No impurity phase was identified in the synthesized sample [17,18].

3.2 Fourier Transform Infrared Spectroscopy (FTIR):

FTIR works on the principle of interaction of infrared light with the vibrational modes of the molecules. FTIR analyses the structural and the chemical property in the Mid IR region 4000cm^{-1} to 400 cm^{-1}. The spectrum was used to observe the functional group, chemical bonds and molecular interaction in material. The FTIR spectrum of synthesized hydroxyapatite and Magnesium doped brucinium hydroxyapatite of higher percentage (2%) is shown figure (2).

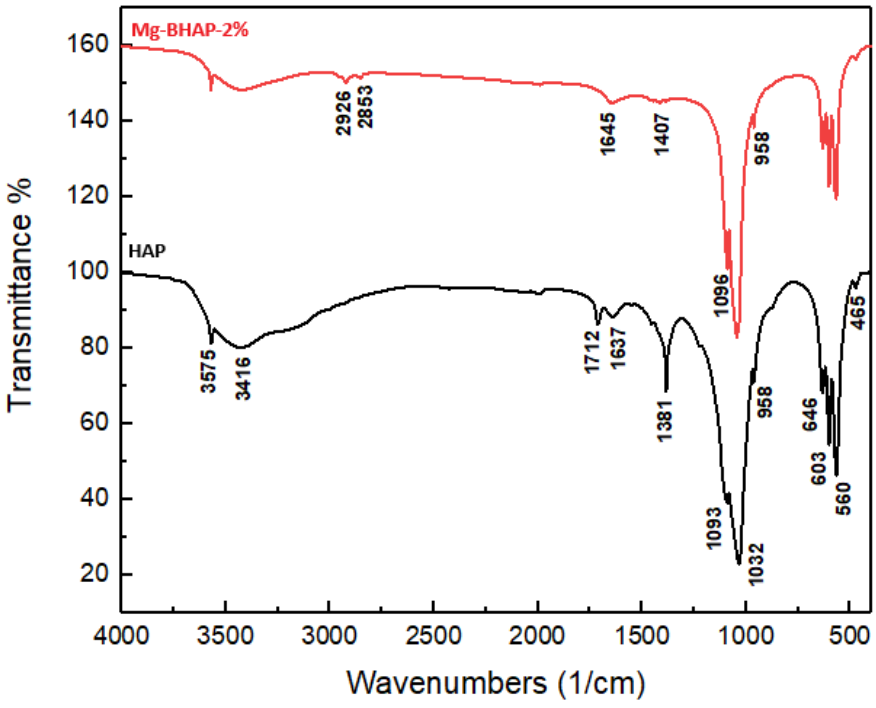

Figure (2) FTIR- Hydroxyapatite and Mg- doped brucinium hydroxyapatite 2%

The peak present at 500–650 cm⁻¹, 958 cm⁻¹, 1032 cm⁻¹, 1093 cm⁻¹, 1381 cm⁻¹, 3416 cm⁻¹, 3575 cm⁻¹ strongly evident the standard HAP. The peak observed at 3400 - 3600 cm⁻¹,1600 - 1720 cm⁻¹ attribute to the water absorption, owe to the high specific surface area

mainly in precipitated powders [17,19]. The band presented at 550 - 650 cm^{-1} corresponds to the bending vibrational mode of P-O of the phosphate group. Whereas, the peak at 958 cm^{-1} tends to stretching vibrational mode. The small peak absorbed at 958 cm^{-1} represents the symmetric vibrational mode of P-O. The peak at 3575 cm^{-1} is due to the presence of O-H. Stretching band present at 1381 cm^{-1}atribitutes to the presence of carbonategroup [19-22]. The peak at 1407 cm^{-1} relates to the stretching -C=O carbonate which occur due to the dopants. The peak absorbed at 2853 cm^{-1} and 2926 cm^{-1} corresponds to O-H vibration due the incorporation of brucine [16]. The FTIR spectrum shows the Mg-BHAP is similar to HAP, however the it changes with the IR wave number of bonds. the resultant FTIR spectrum reveals the no impurity in the synthesised Mg-BHAP 2%. Similar results have been reported in other studies on hydroxyapatite [22-26].

3.3 Scanning Electron Microscopy (SEM):

Scanning Electron Microscope (SEM) indispensable tool, deals with the imaging technique of a beam of electrons focused onto the surface of the specimen interacts with the atom of the specimen and produces the various signals (such as secondary electron, back scattered electron and X-rays) generates a spectrum, which visualize the surface structure, morphology, particle size distribution. The SEM image of Mg doped brucinium hydroxyapatite higher percentage (2%) is shown in the figure (3), offers the information about the shape and size of crystallinity.

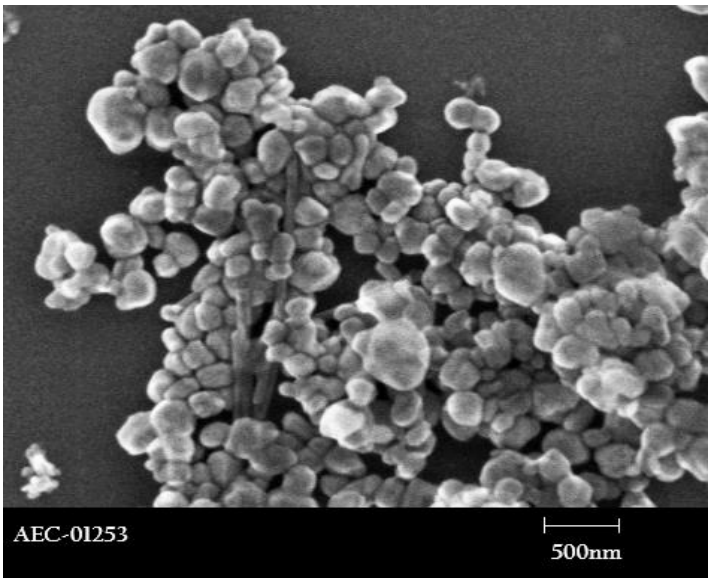

Figure (3) SEM- Mg- doped brucinium hydroxyapatite 2%

The synthesised Mg-BHAP shows the agglomerate and clamped spherical shape due to the incorporation of dopants. Usually,agglomeration occurs due to Oswarld's ripping [27]. The size of Mg-BHAP 2% was about 80-130nm seems to higher when compared to sized obtained in Scherrer equation, due to planes contains carbonated groups are closer to cations of Mg (small) and Ca (larger) [17].

3.4 UV- Visible Spectroscopy (UV):

The UV- VisibleSpectroscopy (UV) is an analytical technique to study the electronic transition in the molecules by the absorption or transmission of UV- visible light onto the sample. The UV spectrum of the synthesized Mg doped brucinium hydroxyapatite of higher percentage (2%) was shown in the figure (4).

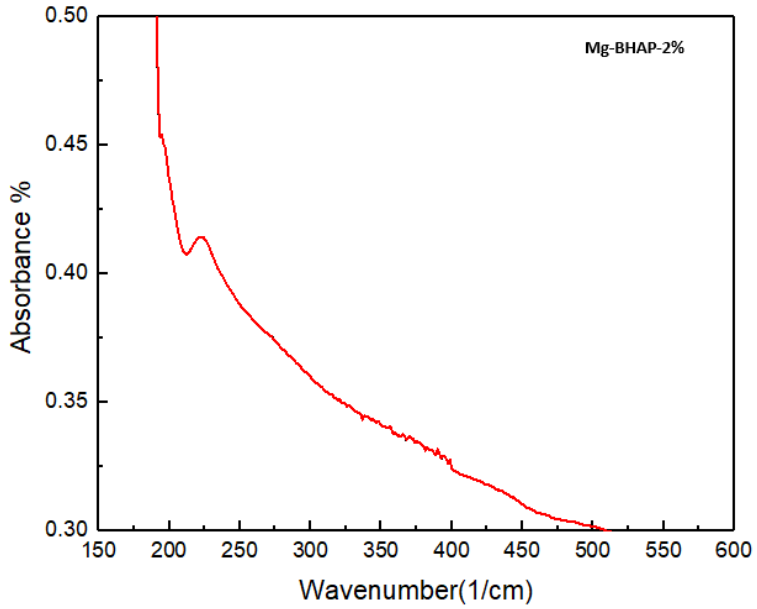

Figure (4) UV - Mg doped brucinium hydroxyapatite 2%

A broad absorbance observed with the low wavenumber band (i.e. 150- 300cm^{-1}) suggest the substantial absorbance which relates to the stuctrual vibration and the distortion in the lattice, the same was supported by the FTIR spectrum. The inclusion of Mg causes the localized defect states and brucine influences the electronic transitions which leads to an increase in absorbance with the range. A notable peak present in the range of 200- 225cm^{-1} aligns with the stuctural appearance and the phosphate vibrarions observed in the FTIR spectrum near 560 cm^{-1}. This peak might arrisrs via improved vibrational interactions among the brucine and HAP stucture as well as electronic modification with in the Mg doped brucininum hydroxyapatite. The absorbance progressively decrases beyond 300 cm^{-1} reflects

the inherent elactronic band gap of the maerial. As reflected by thr FTIR, the functionalized Mg-BHAP with the brucine introduces a red shift with extenting to greater wavelength owes to structural modification and distrotion in the lattice. Further, this behaviour influences the interaction between the organic brucine and the inorganic HAP [16, 28].

Thus, the properties observed in the UV absorbance points the potential of synthesised Mg-BHAP for the applicationssuch as optical filter, Photonic devices , bio-imaging and where the specific wavelength absorbtion is requried.

4. Conclusion:

Magnesium dopedbrucinium hydroxyapatite nanoparticles (Mg-BHAP) of sizeranging from 80 to 130 nm were prepared by a hydrothermal method. The clamped-spherical shaped morphology were noted.The FTIR and XRD analysis revealed the synthesized Mg-BHP matches with the standard HAP. The UV-VIS-NIR optical absorptions obtains the positve approch on electronic and structural modification. Thus, Magnesium doped brucinium hydroxyapatie would a versatile biomaterial for the biological application mainly theonostic and bioimaging.

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