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OPTIMIZE OF THE MECHANICAL AND PHYSICAL PROPERTIES OF HA/B-TCP SCAFFOLD BY USING GENETIC ALGORITHM METHOD

Hassanein Nadhim Abbas[1]*
hassanein.nadhim@yahoo.com
Assistance Prof. Dr. Shaker Jaheel[2]
Assistance Prof. Dr. Mohammed A Ahmed Al-dujaili[3]
Email address: aldujailimohammed@gmail.com
Department of Ceramics Engineering and Building Materials

ABSTRACT

This paper has used the optimization parameters to obtain the maximum compressive strength of scaffold. The porosity and ratio of brushite phase were taken as problem parameters. However, the regression equation was obtained using design of experiment method, also the regression equation which represent the objective function was optimized by using genetic algorithm method. HA/β-TCP scaffold has prepared by using sacrificial method via use of the particle of polymer (PEG) as poregen. The porosity that obtained in the range (40-54%). On the other hand, the best compressive strength by the use of genetic algorithm was 54.67 Mpa, it is approximately on a close with of the experimental value 53.3 Mpa.

Keywords, Biological Hydroxyapatite, β-tricalcium phosphate, Scaffold, Genetic algorithm, Sacrificial method

الخواص الميكانيكية والفيزياوية المثلى للدعامات باستخدام طريقة الخوارزمية الجينية

حسنين ناظم عباس شاكر جاهل ادريس محمد عاصي احمد
قسم هندسة السيراميك ومواد البناء

الخلاصة:

تم في هذا البحث استخدام مفهوم الامثلية للحصول على افضل مقاومة انضغاط للدعامة . المسامية ونسبة طور البروشايت مثلت متغيرات المشكلة ، كما ان معادلة الانحدارقد بنيت باستخدام طريقة تصميم التجربة والتي مثلت معادلة الهدف للخوارزمية الجينية . ان الدعامة من (HA/β –TCP) قد حضرت بخلط مسحوق فوسفات الكالسيوم مع باودر بوليمري (PEG) بنسب مختلفة كمولد مسامات . ان المسامية المتحصلة كانت بحدود (40–54%) ، كما وان افضل مقاومة انضغاط كانت عند (paM54.67) باستخدام الخوارزمية الجينية والتي كانت مقاربة للنتيجة العملية (53.3 paM) .

INTRODUCTION

The reconstructive surgery, repair and regeneration of defective bone is a major challenge. The use of autograft (from the patient) and allograft (from donor) accompanies by multiple complication and risks were associated with the use of both types of graft. However, resulting in worldwide attempts for the development of artificial bone substitute (Bronzino and Peterson 2006) . Thus the development of interconnected porous scaffold plays a significant role in the bone tissue engineering (Antoniac 2012). For this reason, there are several characteristics which are considered to be essential for the bone scaffold, such as biocompactible, osteoconductive and osteoinductive. On the other hand, the osteoconductive scaffold that permit the attachment of cells, growth and extracellular matrix formation of bone related cells on its surface. While, the osteoinductive can actively induce new bone formation. Whilst, the scaffold also should be porous with interconnected porosity to mimic architecture of the bone has suitable mechanical properties. The biodegradable at controlled rate that match the rate of bone formation(Zreiqat, Dunstan et al. 2014). However, the processing routes for macroporous ceramic classified into replica method, sacrificial template, and direct foaming method. Accordingly, there are other procedures which are used to prepare ceramic scaffolds, such as freeze casting(Sultana, Hassan et al. 2014), electrospinning(Boccaccini and Gough 2007). Furthermore, fiber bonding, and poregen leaching (Ikada 2011). In view of that, the modern procedure for the preparation tissues and scaffold are rapid prototyping technologies (Narayan 2014). Hence, Caps have broadly used in the field of biomaterials as bone graft substitutes. This is because, these materials have clinical application in orthopedic, spinal, and maxillofacial surgery. As well, these materials have been regarded as bioactive and osteoconductive, where they bond directly to bone tissue without an interfacial fibrous tissue layer. Additionally, their bioactivity is related to the solubility of cap in physiological media(Ben-Nissan 2014). Subsequently, the most important parameters at calcium orthophosphate are the molar Ca/P ratio, basicity/acidity and solubility. Consequently, the lower the Ca/P molar ratio is more acidic and water soluble, caps with Ca/P ratio of less than 1 are not suitable for biological implantation. But, if the ratio is higher than 1.67 the resorption rate dramatically decrease (Burdick and Mauck 2010), Consequently, the GA based on principle of natural genetics and natural selection and the strongest specimens will survive. As a result, GA regard one of the most successful meta-heuristic techniques for solving combinatorial optimization problems(Terrazas, Otero et al. 2013). Thus, a system using GA produce a variety of(individuals) and select the fittest according to criteria, change the individual, and repeat the process on the next generation (Howard 1995). Accordance with that, GA has applied to wide range of optimization problem from graph coloring to pattern recognition. While, the discrete systems such as travelling saleman problem to continuous system such as the efficient design of airfoil in aerospace engineering. Also, the financial market to multi objective engineering optimization(Yang 2010). However, the GA differs significantly from more traditional search and optimization methods. So, the four most significant differences are; GAs search a population of the points in parallel, it is not a single point, GAs do not require derivative information or another auxiliary knowledge; it is only the objective function and corresponding fitness levels influence the directions of search, GAs use probabilistic transition rules, is not deterministic ones, GAs work on an encoding of the parameter set rather than the parameter set itself (except in where real-valued individuals are used). This study has been used the GA, this is because it is based on the survival of the fittest principles in the nature. Therefore, they maximize the fitness function, also it is suitable for the unconstrained and maximization problems. Additionally, the GA provides a number of potential solutions to a given the problem and the choice of final solution is left to the user.

METHOD AND PROCEDURES

HA/β-TCP Preparation

Ha/β-TCP was produced by solid state reaction by mixing different weight percent ratio (20%, 25%, 30%, 35%, and 40%) of the brushite with HA that derived from bovine bone and calcined at 700°C by ball milling mixing for 1h. While, the mixture was heating in crucible at 1000°C for 3h in furnace. As well, the brushite is first decompose to monotite at 180°C and then decompose to ($Ca_2P_2O_7$) at 340°C which convert to β phase at 700°C according to the following equations:

$$CaHPO_4.2H_2O \longrightarrow CaHPO_4+2H_2O \ldots\ldots \quad (1)$$

$$2CaHPO_4 \longrightarrow Ca_2P_2O_7+H_2O \ldots \quad (2)$$

The obtained $Ca_2P_2O_7$ is wholly reacting with HA to produced mixture of HA/β-TCP in different ratio according to the following equation:

$$Ca_2P_2O_7+Ca_{10}(PO_4)_6(OH)_2 \longrightarrow 4Ca_3(PO_4)_2+H_2O \ldots \quad (3)$$

Scaffold Preparation

The scaffold was prepared by mixing calcium phosphate powders with PEG powder (100-1000µm) in diameter as poregen at different weight percent ratio (3%, 5%, 7%, and 10%). The study has added 2% PVA to bind the mixture and wet PEG powder, increase weight present of PEG over 10% lead to crushing the samples. **Table 1** shows the calcium phosphate with PEG in different mixing ratios, and forming using die pressing method by compacting the powder in steel die of diameter 16.3mm by compression hydraulic device at compaction pressure (200 Mpa) in loading rate(0.5kn/sec). The samples are then dried and heating in 500°C for 2h to remove all the organic material and sintering in 1000°C within 1 hour in rate 16.6°C/min. on reaching 1000°C. The temperature is maintained for 2 hours, then cool down in furnace to room temperature, the sintering program shown in **Fig.1**.

PHYSICAL CHARACTERISTICS

Porosity of Samples

The specimens were tested by Archimedes method according to (ASTM C373-88) method by drying, the specimens in drying oven at 150°C for 24h., then cooling to room temperature. The draying specimen is weighted (D) to nearest 0.01g. However, a place the specimen in glass beaker of distilled water and boil for 5h, and determine the suspended weight(S) after soaked for an additional 24h. Then, remove all excess water from specimens by cotton cloth and record the saturated weight (M). Calculating the apparent volume (V) and volume of open pores (Vop) and impervious volume (VIP) as follow:

$$\boldsymbol{V = M - S} \ldots \quad (4)$$

$$\boldsymbol{V_{op} = M - D} \ldots \quad (5)$$

$$Vip = D - S \ldots \quad (6)$$

The apparent porosity is relationship of volume of open pores to exterior volume and calculate as follow:

$$P = \left(\frac{M-D}{V}\right) * 100 \ldots \quad (7)$$

We can calculate the total porosity (P_t) by following equation:

$$P_t = 1 - \left(\frac{\rho_b}{\rho_{th}}\right) \ldots \quad (8)$$

Where is ρ_b bulk density, ρ_{th} is theoretical density of volume mixture of β-TCP and HA. The theoretical density of β-TCP is 3.07g.cm^{-3} (Zhang 2007)while the density of Ha is 3.156 g.cm^{-3}(Ratner, Hoffman et al. 2012) .

Bulk Density

The bulk density of specimens is calculate after sintering according to ASTM (373-88) by following equation:

$$\rho_b = D/V \ldots \quad (9)$$

MECHANICAL TESTING FOR SCAFFOLD

Compression Strength

The samples was prepared according to (ASTM C773-88), the prepared specimen is cylinder and their diameter is (16.3mm), the compression force calculating using (the hydraulic universal material tester, 50 kn load cell) with compression rate (0.3 kn/sec), the compression strength determine by using the following equation:

$$\sigma = \frac{P}{A} \ldots \quad (10)$$

The mean compression strength is taken for every mixture.

RESULT AND DISCUSSION

Many techniques that used to evaluate chemical composition and crystallization of HA powder that derived from bovine bones, and brushite that prepare by precipitation method and HA/β-TCP that produced by solid state reaction of hydroxyapatite and brushite.The mechanical and physical tests were used to evaluate strength and physical properties of calcium phosphate scaffold , also samples was scanning using SEM to evaluate the microstructure and pore size of scaffold .

XRD Results

Fig. 2. A, B shows the XRD results of A) (HA/brushite) mixture before and after B) heat treatment at 1000°C at 20%brushite ratio, respectively. The appear of β-TCP peak refer to that reaction was occurred between HA and Ca2P2O7. This is form due to the decomposition of

brushite in two steps to form ca2p2o7. For that reason, the peak for $Ca_2P_2O_7$ after heat treatment not exit and this indicate that $Ca_2P_2O_7$ completely reacting with part of HA to form HA/β-TCP mixture. The results have showed that increase in the brushite ratio leads to increase in the β-TCP ratio at the expense of hydroxyapatite ratio due to increase in $Ca_2P_2O_7$ that obtained from decompose of brushite phase.

Physical and Mechanical Results

At 20% brushite ratio addition the apparent porosity 34.11vol% for samples without the addition of PEG, the research has showed that porosity increase from (41.9 to 44.7 vol %) with increase the PEG ratio from (3% -10%) **Table 3**. This indicate that most of polymer addition removed with heating process. **Table 3** as well has showed that the same behavior in increasing the porosity with increase brushite ratio from (20% to 40%). Additionally, the research has observed that there is slightly increase in porosity with increase brushite ratio from (20% to 40%) without the addition of PEG, this is because of the decomposition of brushite. On the other hand, the compressive strength change with variation in volume fraction of porosity and HA/β-TCP ratio, and also effected by pore size, pore morphology and interconnectivity of pores. In **Fig.3** relation between compressive strength and brushite addition. There is an increase in compressive strength from 28.41Mpa to 53.3Mpa with increase brushite ratio from 20% to 25% and this due to the increase in β-TCP ratio which obtained during solid state reaction, and there is slightly decrease in compressive strength at increase the brushite ratio (25% to 40%) and this due to increase the decomposition of brushite at high percentage ratio. Ha/β-TCP mixture have higher mechanical properties than the single phases.(Ruseska, Fidancevska et al. 2006). In this work the average compressive strength of hydroxyapatite that derived from bovine bones that sintering at the same previous conditions at porosity (29.3 vol %) and bulk density 2.225 gm/cm^{-3} was (55Mpa). The compressive strength of hydroxyapatite at particle size 160μm and heating rate 10°C/min and temperature 1000°C with porosity 40% was (35 to 40Mpa)and this close to compressive strength of native bone (Tovstonoh, Sych et al. 2014). **Fig.4** shows the effect of porosity on compressive strength at 20% brushite ratio, the increase in porosity due to addition of PEG at different ratio leads to decrease in all mechanical properties. This is because, it represent a stress concentration on ceramic body, the compressive strength decrease in exponential manner with increase volume fraction of porosity and seem to be the same trend at all ratios of brushite addition as shown in **Table 3**.

SEM Results

Fig.5 shows the SEM result of HA/β-TCP scaffold at 10%, and 5% PEG addition respectively for surface and surface of fracture. It clear that porous microstructure was obtained , and macroporous (d >50nm) with pore size ranging from few micrometers to nanometers ,and the amount of porosity was increased as the PEG content increased due removal of polymeric content during firing and sintering process ,the gaseous products generated from polymeric particle and binder combustion and decomposition process also from evaporation of moisture content contributed to produce pores .

The fracture surface show transgranular fracture with porous microstructure between grains and necks of connection of grains which indication that interconnection pores was produced and this due to sintering condition , PEG content , and the size of polymeric particles. The high sintering temperatures was avoiding and sintering at short holding times to avoid the produce of dense microstructure in conventional pressureless sintering. This is because, the high temperatures are associated with excessive grain growth and decomposition of HA. It has been reported that processing of HA at higher temperatures (exceeding 1250-1450°C) result in exaggerated grain growth and decomposition , while large pores was produced in sintering bodies at 1050°C and significant reduction in porosity at 1250°C (Chetty, et al. , Muralithran and Ramesh 2000).

REGRESSION EQUATION ANALYSIS

The prediction model for compression strength is established by taking compression strength as dependent variable and input variables (porosity, ratio of brushite) as independent variables. Therefore, the design of experiment has used based on 25 experiments for 2 factors and 5 levels **Table 3** using Minitab software, a regression relationship is established between them given in **Eq. (11)**

$$\boldsymbol{\sigma = 52.9 - 137\,P + 452\,rb - 632\,p * rb} \quad .... \qquad (11)$$

Where (σ) is compression strength, (rb) ratio of brushite, and (p) is total porosity.

This analysis in **Table 2** p-value is close to zero, and the R^2 value in statistics is also a key parameter, this is because it indicates model performance. For this reason, R^2=73.89%, R (adj) =70.16% which are considered a good fit between dependent and independent variables.

THE OBJECTIVE FUNCTION AND PARAMETER OF GENETIC ALGORITHM

The first step of the GA is creation of initial population with individuals, each individual represent a possible solution. Then, next step is evaluation of individuals by the use of fitness function. The population is then operated by three GA operators (reproduction, crossover, and mutation) to produce new population of points (Vas 1999) .

The genetic algorithm option in the optimization tool of Matlab software was used to represent solution of the optimization problem. The parameter of GA were as follow:

- The objective function

The objective is maximizing the compression strength with constrained variables, the porosity of scaffold bounded by (40-50), while ratio of brushite constrained by (20-40), also **Eq. (11)** will represent the fitness function.

- Initial Population and number of generation

The population consist of individuals or chromosomes which form the mating pool, the chromosome represented by parameters of problem in this case porosity and ratio will represent the parameters or variables. The population type was bit string and their size was 20 individuals. As the number of generation increases the fitness value of the entire generation increases then stabilized when found the best solution, and the individuals in the population get closer to optimum point the number of generation was 51.

- selection Crossover and mutation

The selection type was stochastic uniform, and the children created by combining the genes from a pair of parents selected on count of Fitness, while each gene represent the variable. The crossover is applied for the parent or chromosomes which contain the variables of problem as gens. The two point crossover is selected and crossover fraction was 80%, the children created by introducing random change or mutation in the gene of a single parent the mutation type was uniform with probability specified by 0.2.

THE OUTPUT SOLUTION

Fig. 6 explains the objective value result in Matlab software which was (54.67Mpa) at the individual value, porosity 40%. Also, the ratio of brushite was between (25 to 30 wt %) which represent the best individual or chromosome as shown in **Fig.7, b**. This is the result it was approximately agreement with experimental value (53.3Mpa) at 40% porosity and 25% ratio of brushite. While, the other factors uncontrolled conditions, such as moisture, presence of agglomerate and the morphology of porosity …etc. it will lead to this difference.

CONCLUSIONS

HA/β-TCP scaffold was successfully prepared using sacrificial method using particle of polymer (PEG) as poregen. The porosity that obtained was in the range (40-54%) and it increase as the percentage ratio of polymer increased. The genetic algorithm optimization was used to optimize of the problem parameters which are involved porosity, and the ratio of brushite phase. The best compressive strength using genetic algorithm was 54.67 Mpa at and it approximately agreement with experimental value 53.3 Mpa and this may be due to uncontrolled condition such as moisture and presence of agglomerates and the morphology of pores and others factors.

Table 1 . Weight percentage of calcium phosphate and PEG at each experiment

Experiments no.	Calcium phosphate powder (wt%)	Peg(wt%)
1.	(80%HA,20%brushite)100%	0%
2.	(80%HA,20%brushite) 97%	3%
3.	(80%HA,20%brushite) 95%	5%
4.	(80%HA,20%brushite) 93%	7%
5.	(80%HA,20%brushite)90%	10%
6.	(75%HA,25%brushite)100%	0%
7.	(75%HA,25%brushite)97%	3%
8.	(75%HA,25%brushite)95%	5%
9.	(75%HA,25%brushite)93%	7%
10.	(75%HA,25%brushite)90%	10%
11.	(70%HA,30%brushite)100%	0%
12.	(70%HA,30%brushite) 97%	3%
13.	(70%HA,30%brushite) 95%	5%
14.	(70%HA,30%brushite) 93%	7%
15.	(70%HA,30%brushite)90%	10%
16.	(65%HA,35%brushite)100%	0%
17.	(65%HA,35%brushite) 97%	3%
18.	(65%HA,35%brushite) 95%	5%
19.	(65%HA,35%brushite) 93%	7%
20.	(65%HA,35%brushite)90%	10%
21.	(60%HA,40%brushite)100%	0%
22.	(60%HA,40%brushite) 97%	3%
23.	(60%HA,40%brushite) 95%	5%
24.	(60%HA,40%brushite) 93%	7%
25.	(60%HA,40%brushite)90%	10%

Table 2 . Analysis of regression equation

Term	Effect	coef	Se coef	t-value	p-value
Constant		27.94	1.74	16.03	0.000
Porosity	-49.10	-24.55	3.66	-6.70	0.000
Ratio	25.92	12.96	2.49	5.21	0.000
Ratio*porosity	-9.51	-4.76	4.56	-1.04	0.309

Table 3 experiments variables with it results

No. of experiment	Porosity (vol %)	Ratio of brushite (WT %)	Compression strength(Mpa)
1.	39.29254	20%	28.41803
2.	41.78916	20%	23.27124
3.	43.21552	20%	19.58491
4.	44.82809	20%	18.0936
5.	45.52036	20%	16.3
6.	41.2756	25%	53.32
7.	43.85346	25%	42.83574
8.	44.57394	25%	30.61803
9.	44.72708	25%	29.30465
10.	47.60899	25%	19.58491
11.	42.0503	30%	49.98675
12.	44.51532	30%	35.77768
13.	46.92993	30%	32.45
14.	47.588	30%	25.63872
15.	51.78152	30%	7.699725
16.	44.33717	35%	48.54006
17.	44.42091	35%	44.5468
18.	44.91411	35%	40.72336
19.	47.28097	35%	31.20337
20.	47.52203	35%	15.40669
21.	44.8227	40%	48.19474
22.	45.37852	40%	43.15328
23.	46.32837	40%	36.71919
24.	49.70557	40%	35.56117
25.	54.24297	40%	15.61087

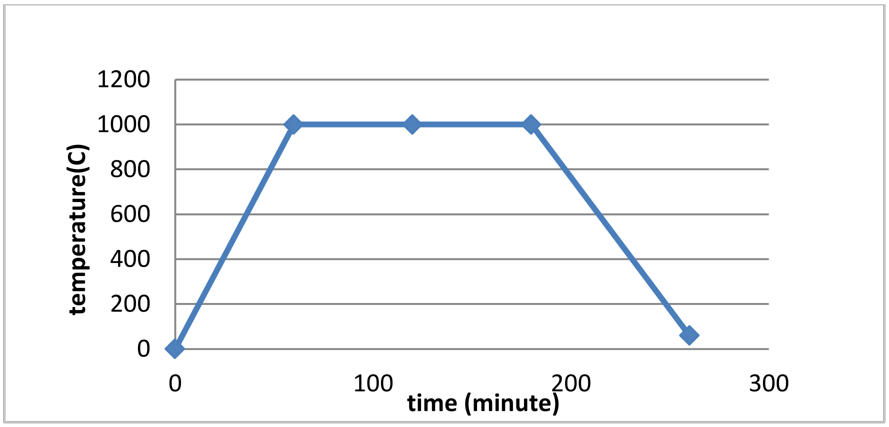

Fig. 1. the program of sintering.

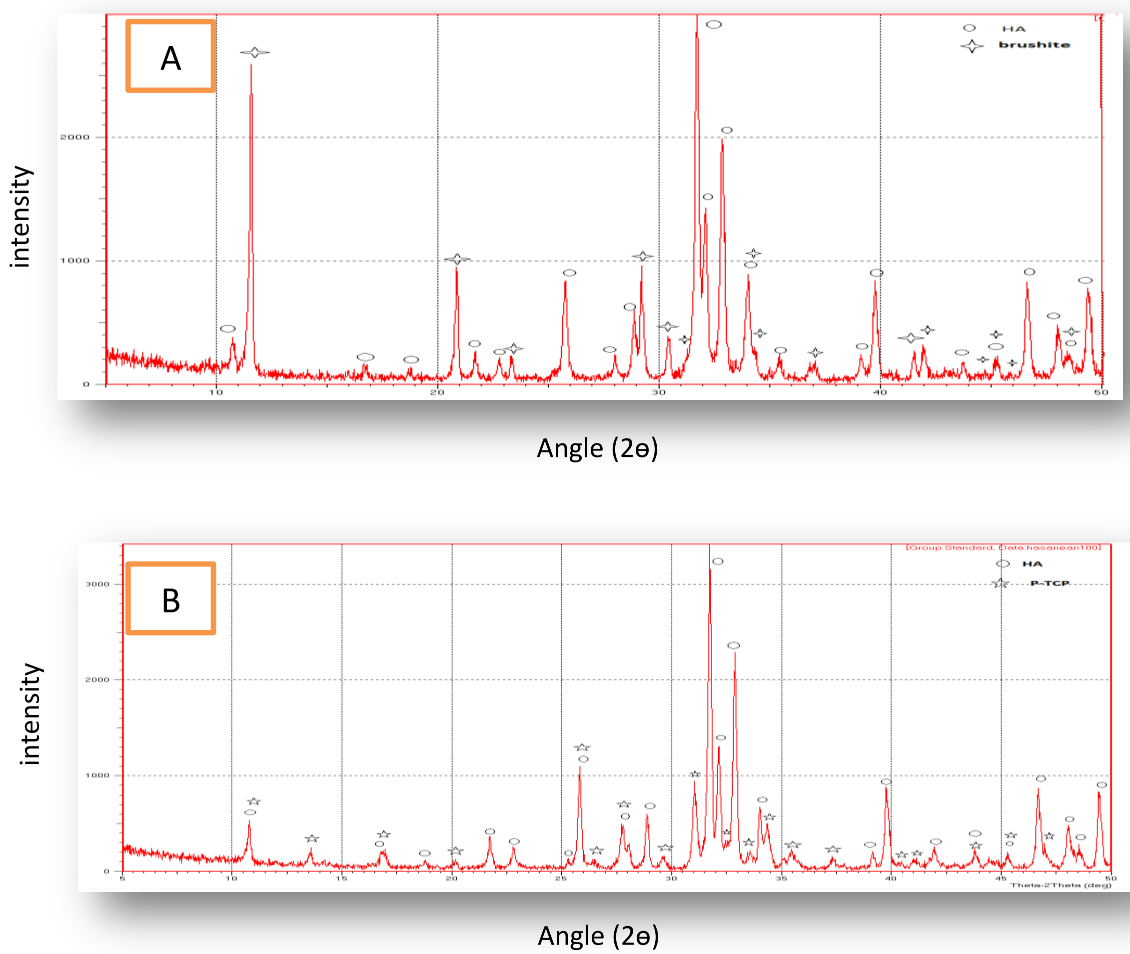

Fig. 2. XRD pattern of (a) (HA/brushite) mixture before and after heat treatment at 1000°C at (b) 20%brushite ratio.

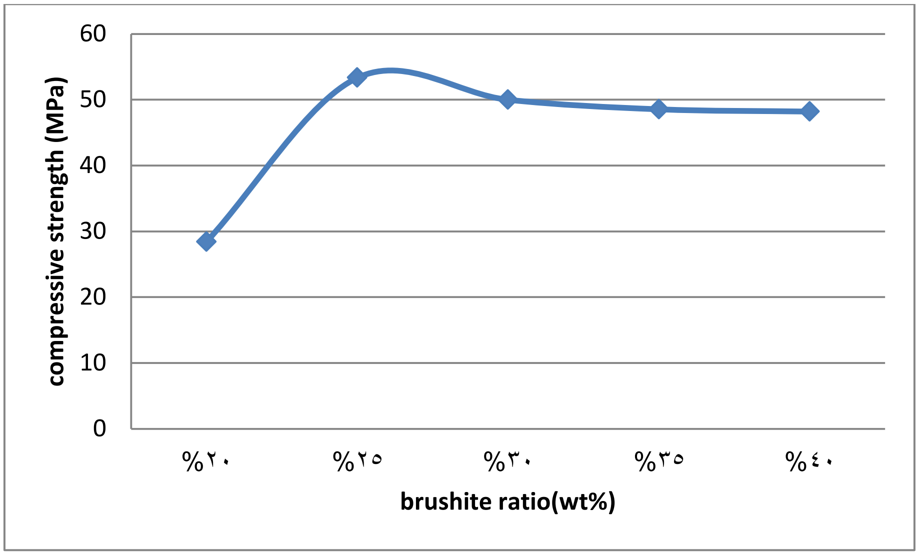

Fig.3. Relation between compressive strength and brushite addition.

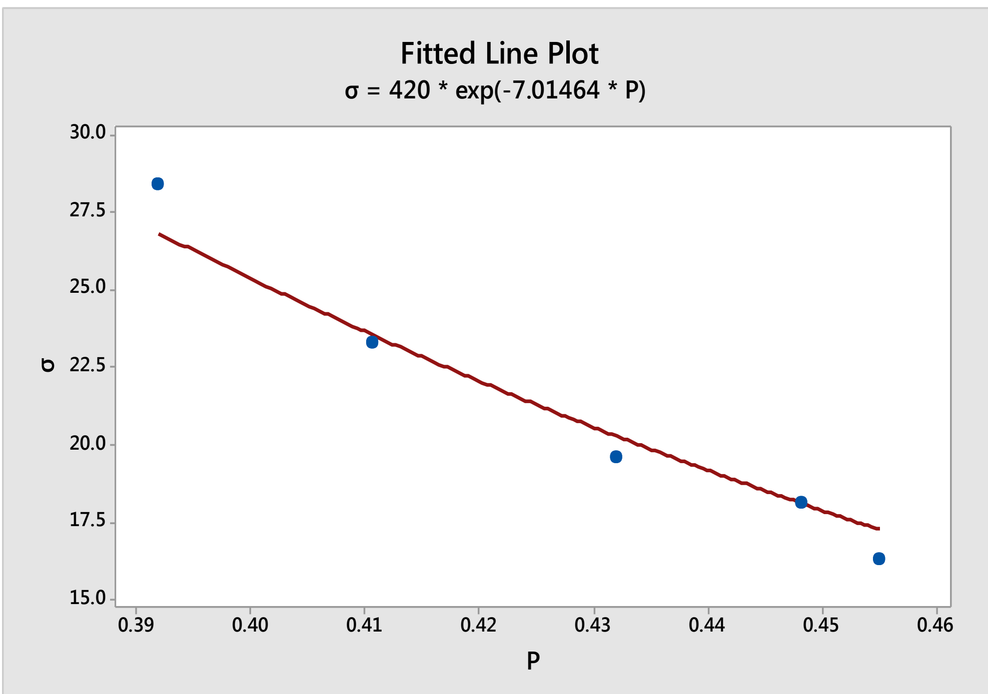

Fig.4. Relation between porosity and compressive strength at 20% brushite

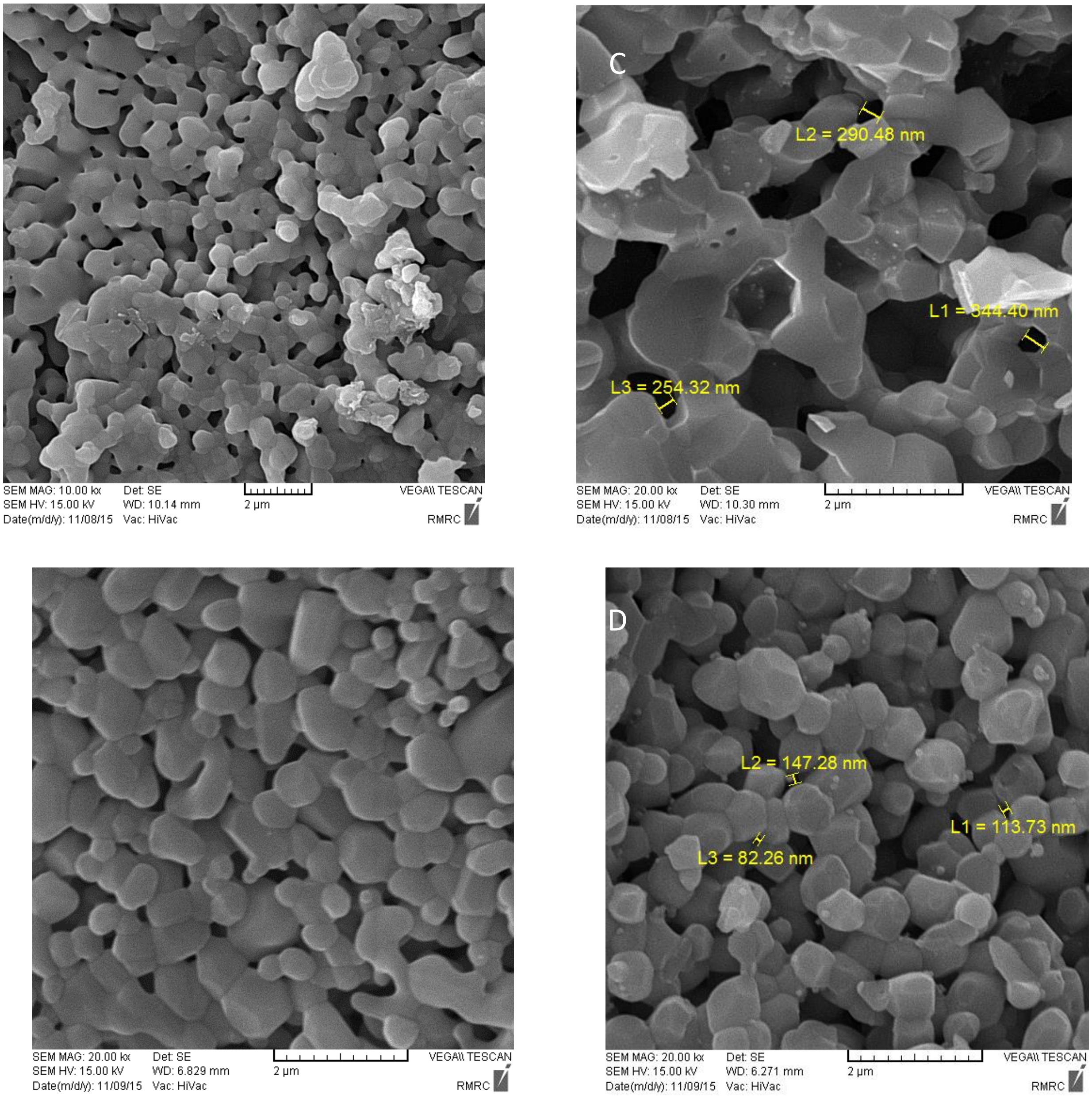

Fig. 5. SEM for HA/β-TCP scaffold for surface at a)10%PEG, b)5%PEG addition, and fracture surface at c)10%PEG , d)5%PEG

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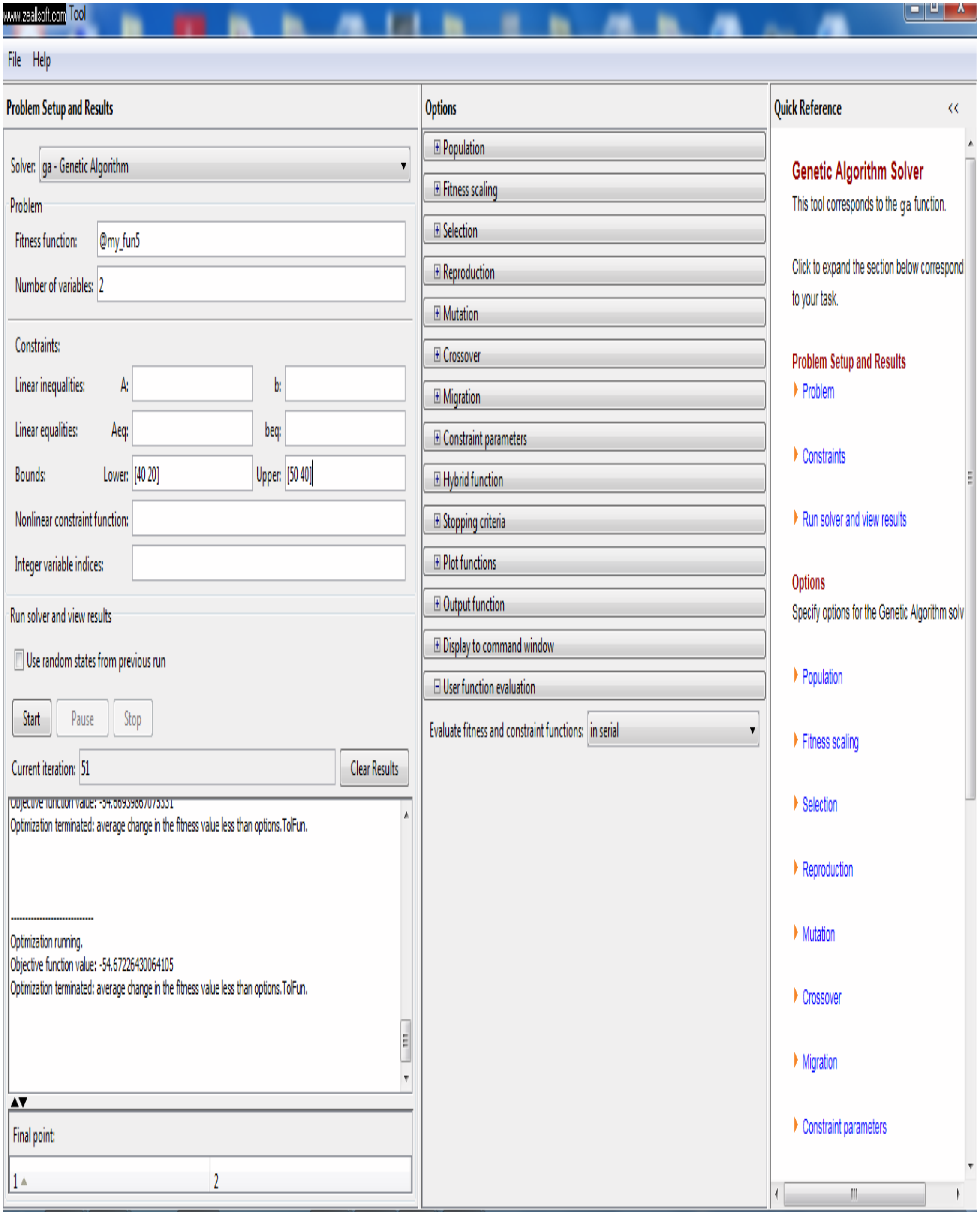

Fig.6. The output solution by Matlab software

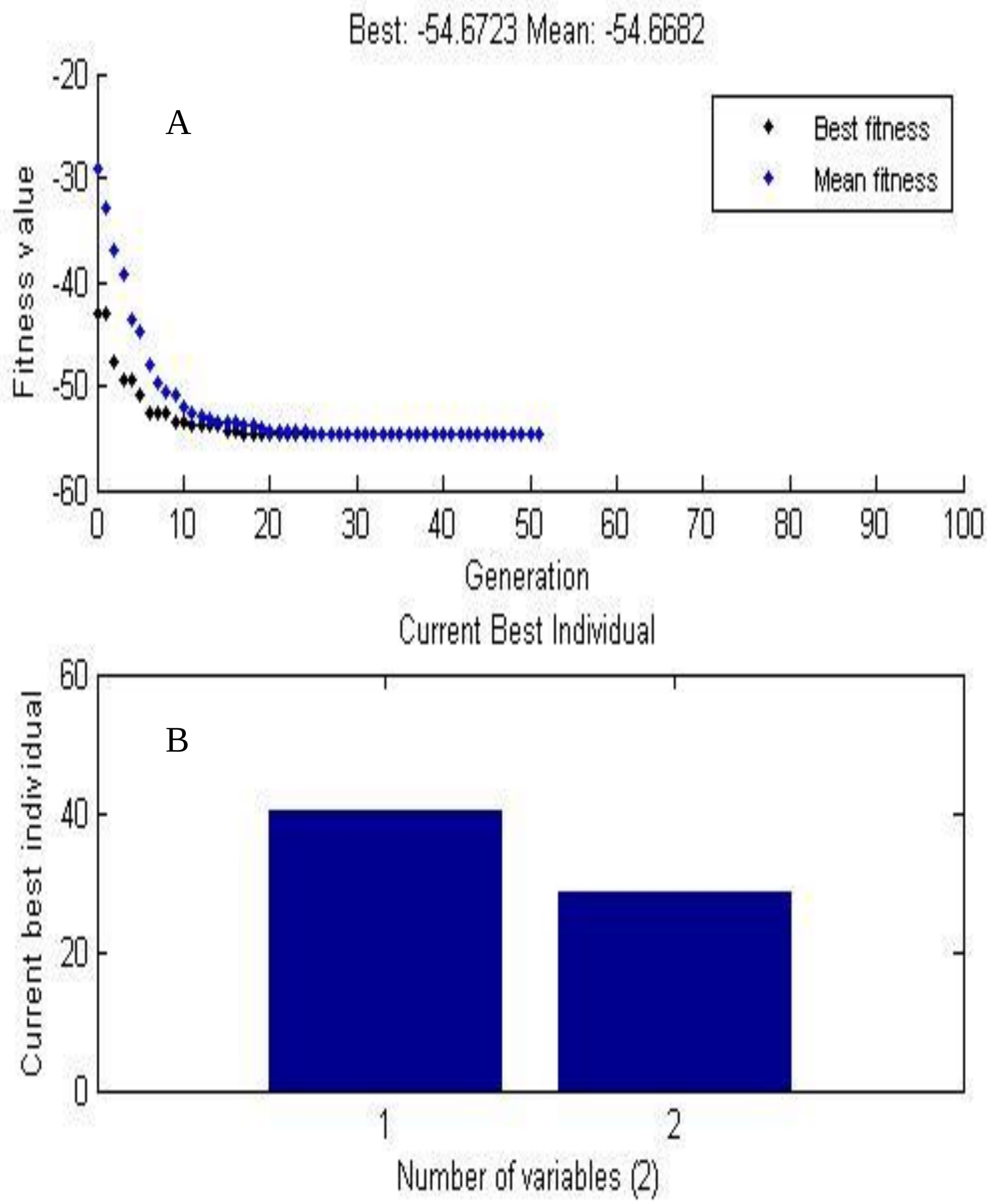

Fig. 7: A. The generation verses the fitness value B. The best individual or chromosome.

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