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Full Length Research Paper

Contribution of Biomimetics to the Development of 4D Printed Hydrogels

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Abstract

Hydrogels are materials capable of absorbing a large amount of water. They can be synthesized using polysaccharides, proteins, synthetic polymers, etc. Usually, these materials are sensitive to external stimuli, which mean that they can change when submitted to a specific environment. For example, they can change their volume due to the pH variation. Because of this sensibility, hydrogels can be used as ink in 4D printing, which is a technology that prints dynamic materials. In other words, it is a printing technique that creates materials capable of changing when there is an external stimulus, such as water presence, magnetic field, heat, etc. This paper approaches the synthesis and behaviour of two types of chitosan/PVP hydrogels and discusses, using bibliographic references of editorial selectivity, if these materials can be used as ink in 4D printing. In addition, there is a theoretical approach to the use of biomimetic concepts in the design of the printed material.

Keywords: 4D printing, additive manufacturing, biomimetics, hydrogels, polymers.

INTRODUCTION

Hydrogels are crosslinked hydrophilic polymers capable of absorbing and retaining a lot of water (typically 70-99%) and other fluids. They usually are derived from polysaccharides, such as chitosan and hyaluronic acid, proteins, like gelatine and collagens, and synthetic polymers, like polyesters [1].

Due to their ability to absorb water, they are applicable to many areas, like drug delivery systems, tissue engineering, actuators, etc. Depending on the applications, there are specific design requirements and this is why biomimetic design is commonly applied, mainly when the use of the hydrogel is in biomedical area [2].

Biomimetics is the inspiration in nature to create some technology [3]. This inspiration can be in the design, properties, behaviour, functions, etc. [4]. This concept is important once natural stuffs have gone through years of evolution and currently are very efficient [5]. For example, for hydrogels application in tissue engineering it is necessary that it has the design similar to the replaced tissue and acts exactly as it. This design can be developed by 3D and 4D printing.

4D printing is similar to 3D printing, but the printed structures are able to transform over time in response to external stimuli, like pH variation. This phenomenon is possible since smart materials (materials that have the ability to change shape, properties, or another condition, under the influence of a stimulus) are used [6].

Experiments involving this type of technology started in 2012 by Skylar Tibbits (MIT) [7], and currently researchers of The Wyss Institute (Harvard) have given attention to the subject, mainly using biomimetic concepts to develop 4D printed materials [8].

The use of hydrogels as ink in this technology is an interesting option once this material is sensible to certain stimuli.

This paper approaches the synthesis of chitosan/PVP hydrogels with different rates between chitosan and PVP. There is also a discussion about how these hydrogels can be used in 4D printing and how bio-mimicry can contribute with this.

MATERIALS AND METHODS

Polyvinylpyrrolidone K30 and Chitosan of Synth, and 25% glutaraldehyde of Sigma-Aldrich were used to develop the chitosan/PVP hydrogel.

METHODS

Chitosan/pvp hydrogel synthesis

To synthesise the chitosan/PVP hydrogel the paper of Risbud et al. was used as base [9,10]. For this, an aqueous solution of acetic acid was mixed with chitosan and placed on a magnetic stirrer for 48 hours. This solution was named as solution 1. Solution 2 consisted in mix distilled water with PVP in a magnetic stirrer for 3 hours.

To form the solutions that would originate the hydrogels A and B, 50 ml of solution 1 was mixed with 50 ml of solution 2 (hydrogel A), and 70 ml of solution 1 was mixed with 30 ml of solution 2 (hydrogel B).

After that, 1 ml of 25% glutaraldehyde was added to both systems and the mixtures were placed in Petri dishes that were dried at 32°C for 72 h.

Analysis of the ph effect in hydrogels swelling

Six samples of hydrogels A and B were collected and their masses were measured in order to compare how hydrogel swells when inserted in water with different pHs. After that, the samples were immersed in pairs for 36 hours in solutions of acid, neutral and basic pH, as shown in (Table 1).

Then, the surface of the hydrogels was dried and the masses were measured again-to determine the percentage of water absorbed using the formula 1:

$$\%water\ absorbed = \left(\frac{Hydrogel\ swollen\ Mass}{Hydrogel\ dry\ Mass}\right) \times 100\% \qquad (1)$$

Literature review about the application of biomimetics in hydrogels 4D printed

A literature review was made to understand if hydrogel 1 or 2 could be used in 4D printing. This review consisted in understand which characteristics the material needs to have to be used in this type of technology. A review of how biomimetic can be applied in the design of these printed materials was also made.

RESULTS AND DISCUSSION

The rheology

During the hydrogels synthesis it was possible to realize that the hydrogel 1 was liquid before being inserted into the stove. But in this same step, hydrogel 2 already had a gel consistency. This aspect is explained by the amount of chitosan used.

Chitosan if formed by the deacetylation of chitin, which is a process that consists in the transformation of the acetamino group (-NCOCH3) into an amine group (-NH2) [11]. The amine group is capable of forming crosslinks, what increases the rigidity of the material. This way, the more chitosan, the higher the rigidity of the hydrogel once the units of amino affect the gelation rate [12].

Hydrogels undergo a reversible phenomenon called the sol-gel transition. Such phenomenon, which consists in the transformation of the material from a fluid phase to a semi-solid phase, and vice versa, occurs in a temperature called of sol-gel transition temperature (Tsol-gel) or gelation temperature. Thus, below the Tsol-gel, the hydrogel is fluid, and above it, it is semi-solid (gel consistency).

This factor demonstrates that, with the increase in temperature, there is greater interaction between the polymer chains, which will interconnect to harden the material. In addition, it is necessary to mention that such temperature depends on numerous factors of the polymer composition, i.e., different hydrogels have different sol-gel transition temperatures [13].

In the case of chitosan/ PVP hydrogel, the greater the quantity of amino groups, the greater the gelation rate and the lower gelation temperature. The synthetized hydrogels are shown in (Figure 1).

The swelling of the hydrogel due to the variation of ph

After the hydrogels were immersed in water (with different pHs), the masses of the samples were measured again. Then, the average masses of the samples that were immersed in

Table 1: Masses of samples collected and pH of Test

Type of Hydrogel	Sample Name	Sample Mass before immersion in solution (g)	pH of Solution
Hydrogel A	HA1A	15,030	acid
Hydrogel A	HA2A	30,440	acid
Hydrogel A	HA1N	22,565	neutral
Hydrogel A	HA2N	30,588	neutral
Hydrogel A	HA1B	27,306	basic
Hydrogel A	HA2B	31,892	basic
Hydrogel B	HB1A	41,736	acid
Hydrogel B	HB2A	18,570	acid
Hydrogel B	HB1N	25,134	neutral
Hydrogel B	HB2N	34,033	neutral
Hydrogel B	HB1B	18,634	basic
Hydrogel B	HB2B	32,295	basic

the same pH were obtained and the percentage of water absorbed was calculated, as shown by (Table 2). Table 2 shows that all samples expanded when immersed in different pHs. This phenomenon can be explained by looking at the chitosan and PVP structures.

Chitosan has amino groups that can protonate and deprotonate, which implies the sensitivity of the hydrogel to pH. When chitosan hydrogel is immersed in a solution with high pH value (above 6), the amino group deprotonates, and when this pH is low (below 6), this group protonates as a quaternary ammonium salt with positive charges [9].

Thus, the material tries to minimize the repulsion of the charges presented in the chemical structure, which implies in the hydrogel expansion [14].

PVP does not have a group that can protonate and deprotonate, so this polymer is not responsible to the pH sensibility of the hydrogel [15].

Thus, it was expected that the greater the chitosan amount, the greater the swelling of the hydrogel. This behaviour happened as expected. Therefore, it is possible to conclude that chitosan/PVP hydrogels can be used in 4D printing, theoretically, once this type of technology uses sensible materials (materials that change over time) to create dynamic devices [16].

Hydrogels 4D printed

3D Printing, also called as additive manufacturing, has been developed in the 80s. This type of technology prints a static material, that is an object that won't change even when submitted to different environments [17]. 3D printer is able to print drones, parts of a robot, another 3D printing, etc. [18]. Therefore, 4D printing comes up to amplify the print applications once it uses sensible materials that can change their properties, shape, etc., when an external stimulus is applied [17,19] approaches that 4D printing consists in using additive manufacturing technology to build a stimuli-responsive object, applying the sensible material, layer by layer, until form an object that can react to stimuli, resulting in a physical or chemical change [19].

Materials such as hydrogels, shape memory polymers, dielectric elastomers, etc, are commonly used in this technology once they are, generally, sensible to stimuli [7]. This stimulus can be temperature, water, pH variation, magnetic field, etc. [20].

A limitation in the use of hydrogels is their low mechanical resistance but in the last decades researchers have developed resistant hydrogels that can form complex structures by 4D printing [21].

Temperature variation is a stimulus that can make the material fold, shrink or swell, depending on their phase-transition temperature. An example of a thermo responsive hydrogel is the poly (N-isopropyl-acrylamide) (PNIPAAm) hydrogel. Developed a bilayered construct printed of PNIPAAM and poly (e-caprolactone) (PCL), which is a water-insoluble polymer. This material is capable of folds or unfolds, depending on the temperature [21]. This behaviour will be approached with more details below.

Water presence is also a common stimulus and the hydrogel deformation is based on the level of water sorption. PEG hydrogel is a material sensible to that stimulus [21]. Developed a bilayered construct printed of PEGs with different molecular weights and that, consequently, absorb different amounts of water [22].

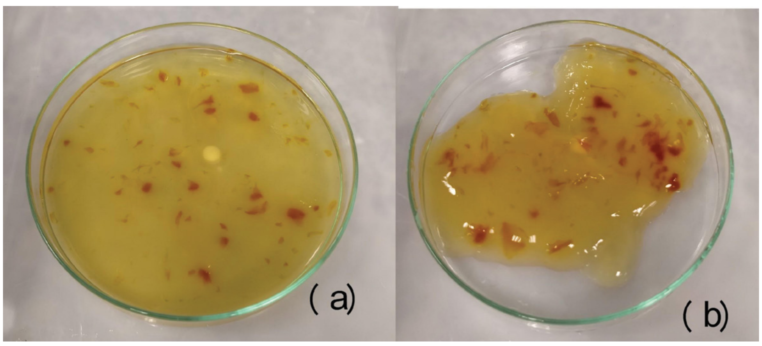

Figure 1: Hydrogel A (a) and B (b) before being inserted into the stove. Source: Prepared by the authors

Table 2: Relation between the mass of dry and swollen hydrogels

Sample Name	Average Mass of the Dry Hydrogel (g)	Average Mass of the Swollen Hydrogel (g)	pH	% water absorbed
HAA	22,735	82,776	acid	364%
HAN	26,577	101,585	neutral	382%
HAB	29,599	111,860	basic	378%
HBA	30,153	128,863	acid	427%
HBN	29,584	120,519	neutral	407%
HBB	25,465	98,933	basic	388%

Both hydrogels approached in this paper were sensible to pH variation, so they can be considered as a sensible material. This way, they are an option to develop a 4D printed material, but other factories are fundamental to understand if they could be used in this technology.

For example, hydrogel B already presented gelatinous consistency during its preparation (before being inserted into the stove), which difficult its manipulation. Thus, its application in 4D printing would probably not be ideal due to the conformation problem before the material being inserted into the stove.

However, hydrogel A was liquid during its preparation, which allows its manipulation into the desired design during 4D printing. In addition, after being submitted to the stove, the material reached a gelatinous consistency, that is, it became more stable, allowing a specific and controlled design.

Therefore, it is possible to conclude that both hydrogels could be used in 4D printing, theoretically. But other aspects, as its rheology, need to be compatible with the technique, enabling material handling during printing, and stability upon printing.

Application of biomimetics in 4D printing

The biomimetic concept can be used to develop the 4D printed structures design used the structure of a flower as inspiration to develop the design of a material that could be printed using a 4D printer. The researcher used a material composed of PNIPAAm hydrogel and PCL to understand how the material would behave in response to temperature [21].

They developed a motel of a flower which has an outer layer of PNIPAAM, a thermo responsive polymer that absorbs water at low temperatures, and an inner layer of PCL, a hydrophobic material. This way, when the temperature is high, both materials won't absorb water, so they have the printed shape. But when the temperature is low, PNIPAAm absorbs water, swell and make the object blend [21].

Gladman et al. [22] was inspired by a plant (a native calla lily flower), which morphology is affected by the amount of water absorbed, to develop a hydrogel composite ink (with cellulose fibrils into an acrylamide matrix, mimicking the plant walls) that would be used to form 4D printed structures. This way, the design was planned and then the biomimetic structure was printed. After that, the printed material was immersed in water and, because of the differences in local swelling, the structure got the shape curved [22].

CONCLUSION

The chitosan/PVP hydrogels synthesized exhibited sensitivity to pH and that is why they could, theoretically, be used in 4D printing once this technique uses sensible materials (materials that change over time) as ink. But, rheological analyses about the aspects of the hydrogels are necessary to understand if this application is possible or not. Therefore, it was possible to conclude that hydrogel B probably can't be used in 4D printing once the material has already presented gelatinous consistency during its preparation, what difficulties its conformation during the printing. However, hydrogel a presented liquid consistency during the preparation and gelatinous consistency after being inserted into the stove, what indicates that is possible to print the material and, after that, put it into a stove to stabilize the material design.

In addition, biomimetics can be used as a design inspiration in 4D printing. For example, when the will7 be applied in the biomedical area, the printed object needs to act exactly like the natural member to be efficient.

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