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I. GRĂDINARU[1*], B.-I.CIUBOTARU[2,3], M. DASCĂLU[2*]

PRELIMINARY STUDY CONCERNING THE ADAPTATION OF A PERIODONTAL DRESSING MATERIAL TO THE INCLUSION OF THERAPEUTIC AGENTS

The aim of this study was to analyze how a periodontal dressing material (COE-PAK, C-P) adapts to the addition of therapeutic agents (allantoin and pyridoxine), especially in terms of its mechanical properties, as these improvements would be very beneficial for those patients going through the healing process. The physical and mechanical characteristics of periodontal dressings have been assessed in a limited number of trials, their clinical application being favorable in some cases, as the surgical periodontal treatment result is thought to be significantly influenced by a variety of factors, one of which is the periodontal dressing. Dental materials and technologies are evolving now faster than ever thanks to the digital era we are living through, but even with these developments the dental medical field, not unlike other medical fields, requires patient-oriented services.

Keyword: Dental materials; periodontal dressing; mechanical properties assessment

1. Introduction

Periodontal dressings represent dental materials applied to the surgical incisions in the oral cavity in order to support the wound healing process and protect the wound sites. They are frequently used during periodontal procedures or following tooth extractions. The ease with which periodontal dressings may be adjusted and inserted into the surgical site, as well as their ability to form a barrier that shields the area from germs and food particles are their two most crucial qualities. In dental medicine, there are two main categories of periodontal dressings: non-eugenol and zinc oxide-eugenol (ZOE) dressings. Eugenol, a natural anesthetic and antibacterial, and zinc oxide are the main ingredients of ZOE dressings. Polyurethane and polyvinyl acetate are only two examples of the materials used for non-eugenol dressings, these materials being indicated for those patients with eugenol allergies [1-5].

The fact that non-eugenol periodontal dressings are efficient in reducing bleeding after dental procedures has given them the recommendation as hemostatic materials. These types of materials function at the surgical site by creating a physical barrier that aids in stabilizing the blood clot and limiting excessive bleeding. Hemostatic materials are used in various healthcare fields other than dentistry, notably in surgeries. In a variety of surgical procedures, such as orthopedic, plastic, and cardiovascular operations, they are utilized to reduce bleeding. They are further used in the emergency care for managing bleeding from severe wounds [6-8].

Periodontal dressings need to be mechanically characterized in order to identify their physical characteristics, which are essential in determining the extent to which they can treat periodontal conditions. Elasticity, tensile strength, tear resistance, and flexibility are some of the crucial factors taken into consideration during mechanical characterization. With the use of these criteria, the dressing's capacity to follow the shapes of the teeth and gums, endure the stresses of chewing and speaking, and preserve its integrity during the healing process may be evaluated [9,10]. The dressing‘s mechanical characteristics are subsequently translated into a recommendation of its use in various therapeutic settings. For instance, a very tear-resistant dressing would be favored for use in places with strong pressures of mastication, like the back teeth, whereas a highly elastic dressing might be selected for use in areas with great movement, like the tongue or lips [11,12]. Moreover, when assessing the suitability of a periodontal dressing for a given clinical circumstance, additional factors like biocompatibility, antimicrobial

[1] "GRIGORE T. POPA" UNIVERSITY OF MEDICINE AND PHARMACY, FACULTY OF DENTAL MEDICINE, DEPARTMENT OF IMPLANTOLOGY, REMOVABLE DENTURES, TECHNOLOGY, 16 UNIVERSITY STREET, 700115, IAȘI, ROMÂNIA
[2] DEPARTMENT OF INORGANIC POLYMERS, "PETRU PONI" INSTITUTE OF MACROMOLECULAR CHEMISTRY, ALEEA GRIGORE GHICA-VODĂ, 41A, 700487, IAȘI, ROMÂNIA
[3] "GRIGORE T. POPA" UNIVERSITY OF MEDICINE AND PHARMACY, FACULTY OF MEDICAL BIOENGINEERING, DEPARTMENT OF BIOMEDICAL SCIENCES, 16 UNIVERSITY STREET, 700115, IAȘI, ROMÂNIA

* Coressponding authors: irina.gradinaru@umfiasi.ro; amihaela@icmpp.ro

properties, and ease of placement and removal must also be taken into account. The efficiency and safety of periodontal dressings in treating periodontal diseases are largely dependent on mechanical characterization [12,13].

Several plants, including comfrey, chamomile, and aloe vera, naturally contain the compound allantoin. Due to its numerous advantageous qualities, allantoin is frequently used in cosmetic and therapeutic products. Allantoin has a number of beneficial qualities, including the capacity to promote skin cell regeneration and improve hydration. Additionally, it has anti-inflammatory qualities that can help lessen swelling and redness. Allantoin is suitable for use in a variety of different products being non-toxic, non-allergenic, and non-irritating [14-16]. Given that it has been demonstrated to quicken the healing process, allantoin can be important for wound healing. It has keratolytic properties, which enable it to disintegrate dead skin cells and aid in removing them from the wound. Additionally, it encourages faster and healthier cell growth, which speeds up wound healing and minimizes scarring [17]. The value of allantoin in wound healing has been addressed in a variety of scientific studies. Overall, these properties indicate that allantoin may be a useful component of products used to treat wounds.

The vital water-soluble vitamin pyridoxine, known as vitamin B6, is necessary for the metabolism of amino acids, the creation of red blood cells and the synthesis of neurotransmitters [18]. The capacity of pyridoxine to take part in enzymatic processes including amino acid metabolism, neurotransmitter production and glycogen breakdown is one of the compound‘s key characteristics. In addition, pyridoxine is crucial for preserving immunological function, controlling homocysteine levels, and promoting the health of the cardiovascular and neurological systems [19,20]. Because it is essential for the formation of collagen, the protein that gives skin, bones, and other tissues their strength and support, pyridoxine is important in the wound-healing process. Additionally, it helps in promoting angiogenesis, the development of new blood vessels that supply healing tissues with nutrients and oxygen [21,22].

Given the applications of periodontal dressings and the properties of allantoin and pyridoxine, our study was based on the medical cause-effect principle, where an identified clinical problem must have a solution. Noting that at this clinical stage some problems (lesions, wounds) persist, we tried adding a therapeutically active agent for the first time in a periodontal dressing and analyzed how well such types of materials are compatible. As such, the aim was to analyze how a periodontal dressing material (COE-PAK, C-P) adapts to the addition of therapeutic agents, especially in terms of its mechanical properties. For this purpose, three materials, two enriched (one with allantoin and one with pyridoxine) and a reference sample, were prepared and characterized in terms of mechanical behavior (elongation at break and compression resistance), swelling behavior in phosphate buffer solution of 6.8 pH and ethanol, and morphology.

2. Experimental

2.1. Materials and methods

The periodontal dressing used in this study was COE-PAK, a non-eugenol product bought from GC Australia [23], prepared and used as instructed by the producers, in a clinical environment, by combining equal lengths of the contained base paste and catalyst and shaping the material into a disk form named **C-P**, of 0.5 mm thickness as shown in Fig. 1 (left) for analysis purposes. Allantoin ($C_4H_6N_4O_3$), Mw = 158.12 g/mol, has been purchased from Sigma Aldrich, and mixed with the periodontal material before repeating the process in order to reach the circular shape of 0.5 mm thickness as well, named **C-P+A**, as shown in Fig. 1 (middle). Pyridoxine ($C_8H_{11}NO_3$), Mw = 169.18 g/mol, has also been purchased from Sigma Aldrich and added to the material as such, repeating the mixing and molding processes as done for the other two materials. Another circular-shaped material was obtained, with a 0.5 thickness, named **C-P+P**, shown in Fig. 1 (right). As it can be seen in the images presented in Fig. 1, the obtained materials have very similar consistencies, no separation has occurred during the mixing process or by molding. All three materials were flexible enough for a very easy manipulation, with no visual differences between them.

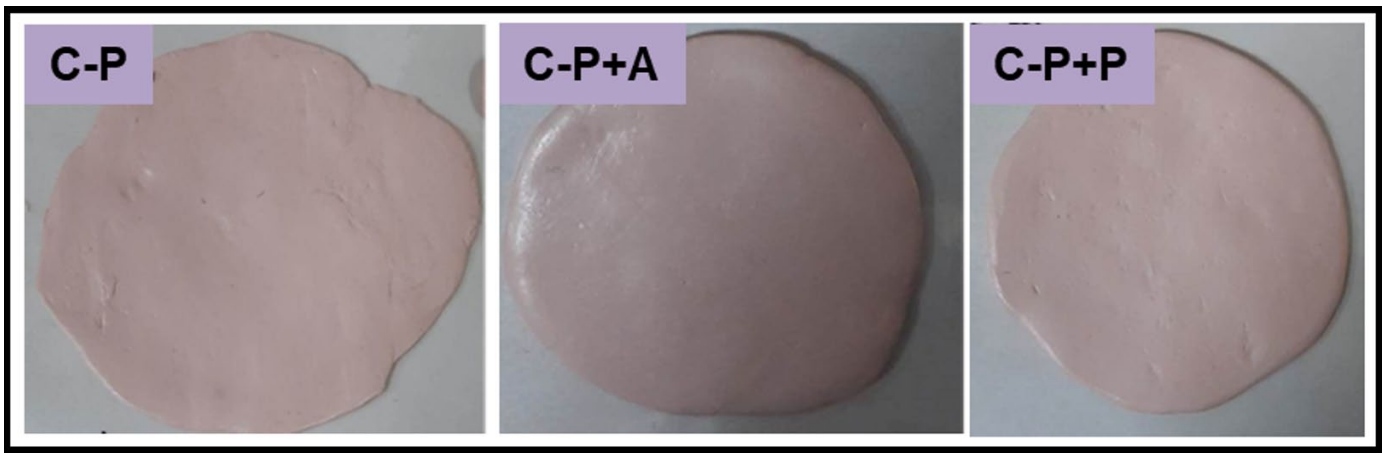

Fig. 1. Periodontal Dressing Materials After Preparation

3. Results and discussion

3.1. Mechanical characterization

A 500 N load cell-equipped Instron 3365 machine was used for the tensile and compression testing. Dumbbell-shaped test specimens of 4 mm in width and 50 mm in length were cut from the materials and used for the tensile testing. The crosshead speed used for the tensile testing was 10 mm/min. Fig. 2 depicts the stress-strain curves that were obtained after the samples underwent linear tensile tests, while TABLE 1 provides a summary of elongation at break, stress at break and Young modulus values at 5%, calculated from the slope of the stress-strain curve by applying a linear fit to the data points in the 0-5% strain range.

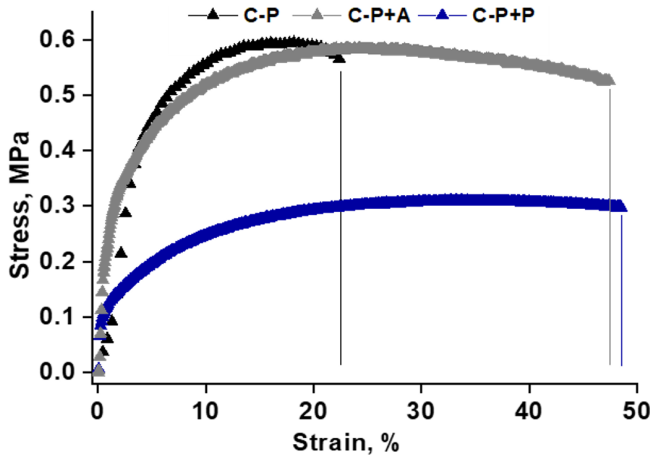

Fig. 2. The Stress-Strain Curves of the Enriched Periodontal Dressing Materials **C-P+A** and **C-P+P** as Compared to the Reference Sample **C-P**

TABLE 1

Mechanical characteristics of the studied periodontal dressing materials

Sample	Elongation at break, %	Stress at break, MPa	*Y*, MPa*	UTT, kJ/m^3**
C-P	22.37	0.57	9.23	0.111
C-P+A	47.47	0.52	8.63	0.251
C-P+P	48.55	0.30	3.98	0.133

* Youngs modulus (calculated at 5% elongation);
** Tensile toughness (calculated as the area from the stress – strain curve).

The **C-P+A** and **C-P+P** materials present higher deformations at break, doubled compared to the reference sample, being softer than **C-P** with lower values of *Y* (2.38 MPa for **C-P+P**, 8.63 MPa for **C-P+A**). The obtained results indicate that added therapeutic agents act as softeners, improving the mechanical behavior of the materials. These results are sustained by literature data which states that the addition of therapeutically active agents lead to softer, less stiff and uncomfortable materials [24]. Periodontal dressing materials usually aid in the healing process, stabilizing wound tissues and reducing pain when applied [25], and while these are ideal properties sought for, there are still challenges in this field. The obtained results are in line with these requirements. The softener role of the therapeutic agents is supported by the toughness values (Eq. (1)), which are higher for the enriched periodontal materials, compared to the reference sample (TABLE 1). All materials present higher deformations at break starting from 22% in **C-P** and reaching 47% for **C-P+A** and ~ 49% for **C-P+P**.

$$UTT = \int_0^{Sm} T_{nm}\, dS \tag{1}$$

Additionally, compression tests were performed on the Instron 3365 machine equipped with the load cell of 500 N. The purpose of the compression testing was to investigate how the materials would respond to compression, at a rate of 50 mm/min, and 10% compressive strain, for 10 cycles of compression each. This measurement is important in assessing how periodontal dressing materials, being often applied in the oral cavity for longer periods of time, behave while chewing or talking.

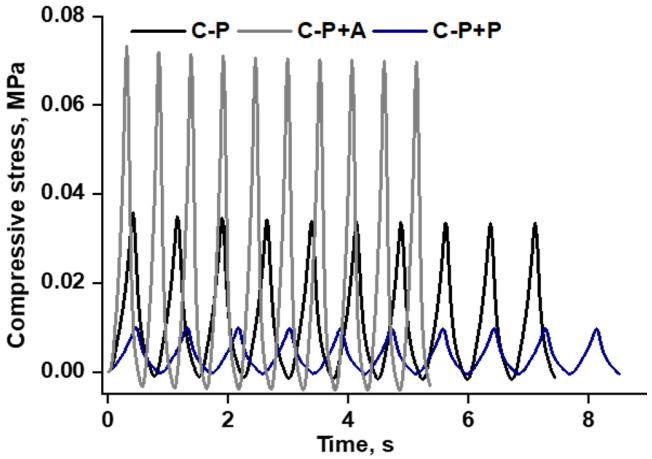

Fig. 3. Compressive Stress at 10% Compressive Strain Comparatively for the Reference Sample **C-P** and Enriched Samples **C-P+A** and **C-P+P**

Fig. 3 indicates a viscoelastic behavior of the samples, these being stable the whole testing time with small variations. The Mullins effect could be responsible for the small variations within the initial compression cycles. The compression resistances are as follows: **C-P+A** > **C-P** > **C-P+P**. The values recorded after the first compression cycle indicate resistances of 0.035 MPa for **C-P**, 0.072 MPa for **C-P+A**, and 0.01 MPa for **C-P+P**. The resulted values obtained for the periodontal enriched materials are similar to the **C-P** one.

3.2. Swelling Behavior Characterization

The solutions that periodontal dressings come into contact with include saliva, blood and gingival fluids, all of which have varying pH levels. Blood has a pH of around 7.4, while saliva's pH ranges from 6.2 to 7.6. Gingival fluids, on the other hand, can have a pH that can fluctuate from slightly acidic to alkaline, depending on the level of inflammation. As a result, without

compromising its structural integrity, the dressing material must be able withstand exposure to liquids with varying pH values.

The materials' degree of swelling was assessed in a phosphate buffer solution (PBS) solution with a pH of 6.8 (in order to simulate the salivary fluid) and ethanol (as the sterilizing process that is advised for the materials recommends). To mimic physiologic conditions, 50 mg samples of each material were immersed in 5 mL solutions and then maintained at 37°C. Eq. (2) was used to calculate the swelling degree by the gravimetric approach.

$$SD(\%) = \frac{Mt - M_0}{M_0} \times 100 \quad (2)$$

where SD (%) – represents the swelling degree, Mt – the material weight at different measured times, and M_0 – the initial measured weight of the material.

Measurements for the materials were carried out over the course of 120 h, as can be seen in Fig. 4. For a good accuracy, at precise times, as indicated on the figure, the measurements were done in triplicate.

It can be observed that higher values of swelling were obtained for the samples immersed in PBS than for those immersed in ethanol. Regarding the swelling in PBS, in the first 2 h, the **C-P** reference material swelled the most compared to the other materials enriched with therapeutic agents. After 4 h, the **C-P+A** material reached a similar value as the **C-P** reference material, and the **C-P+P** showed the least swelling, reaching a plateau after 8 h, while the other materials after 12 h. In this media, the swelling order is: **C-P+A** > **C-P** > **C-P+P**.

The swelling degree order in ethanol followed the same trend, with the **C-P+A** sample swelling the most, followed closely by the **C-P** sample, and the least swelling being observed for the **C-P+P** sample. The higher degree of swelling of the allantoin-enriched material might be due to the hydrophilic nature of allantoin.

3.3. Characterization of Scanning Electron Microscopy (SEM)

A Verios G4 UC Scanning electron microscope (Thermo Scientific, Czech Republic) was used to assess the morphology of the examined materials. Using a Leica EM ACE200 Sputter coater, 10 nm of platinum was applied to the samples to give the

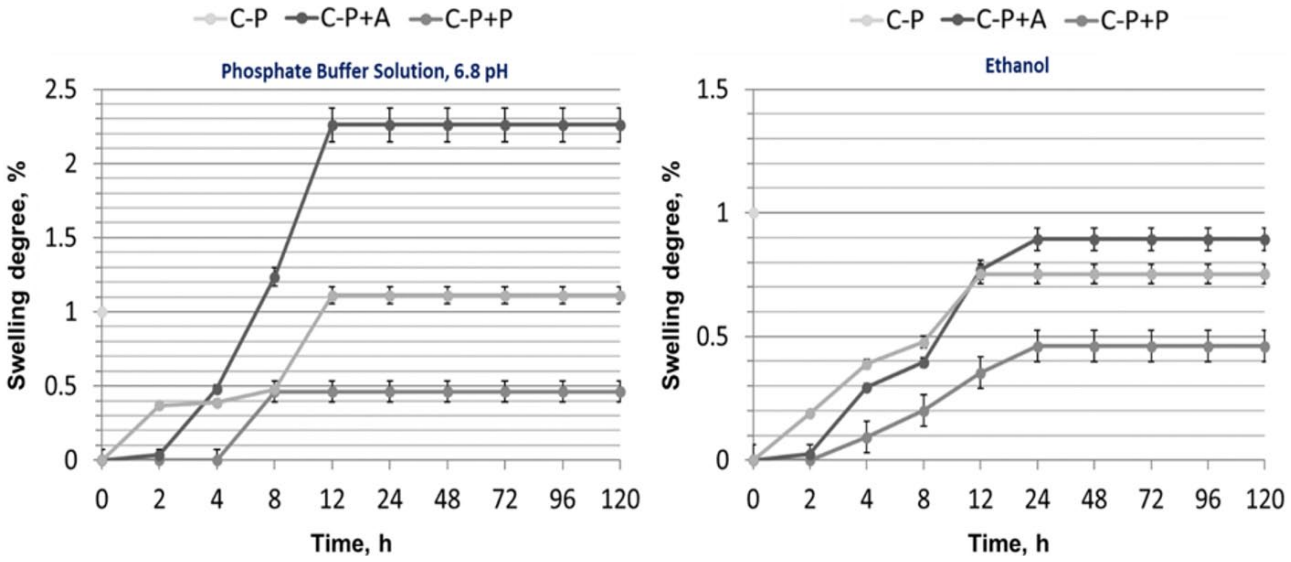

Fig. 4. Swelling Degree of the Samples in PBS Media of 6.8 pH (left) and in Ethanol (right)

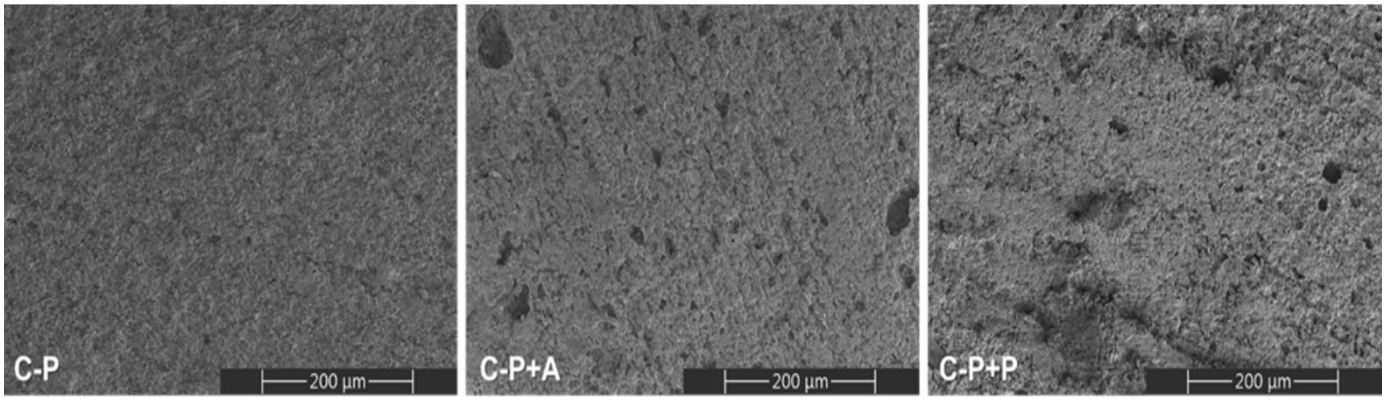

Fig. 5. SEM Images of the Periodontal Dressing Materials on Surface (200 µm scale)

necessary electrical conductivity and avoid charge accumulation while they were exposed to the electron beam. Using a secondary electron detector (Everhart-Thornley detector, ETD) and an accelerating voltage of 5 kV, SEM tests were carried out in the High Vacuum mode.

The surface morphology of the dental materials was examined by SEM microscopy (Fig. 5). The most homogenous sample analyzed through SEM was the reference **C-P**, which showed a compact morphology. In the other materials that included the therapeutic agents, pores of various dimensions were formed, but their presence did not significantly modify the morphology, as they were well dispersed through the periodontal dressing material.

4. Conclusions

Three periodontal dressing materials were prepared and characterized in terms of mechanical properties, swelling behavior and morphology. Allantoin and pyridoxine were successfully added to a periodontal dressing material, resulting homogenous materials. The presence of therapeutics agents influences the mechanical properties, leading to a significant increase of elongation at break and decrease of Young's modulus values. The presence of allantoin in the periodontal material improves compressive resistance, also providing the highest swelling in both tested media, followed by the reference sample and the pyridoxine-enriched material. SEM analysis revealed homogenous consistencies, with some pores formed in the enriched materials. The obtained results indicate that the enriched materials have enhanced properties, thus recommending them for further characterization and analyses.

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