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Revolutionizing Wound Care: Biocompatible Films for Advanced Wound Healing

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Abstract
Traditional wound healing methods struggled with active tissues enduring ongoing motion and biocompatibility. The core objective of this study is to engineer a series of PVA-based wound-healing films containing different additives like acetic acid, Magnesium and Alpha-ketoglutarate. In-vitro tests like swelling, degradation, contact angle, pH sensitivity and moisture content were performed to assess the biodegradability, biocompatibility, hydrophilicity and hygroscopicity of the samples. For in-vivo use, film reactions in the body and excretion time are crucial, whereas hydrophilicity and hygroscopicity would determine the adhesion of the films to the wound and potential inflammatory reactions it may cause. Among the four experimental samples (PVA, PVA/AcOH, PVA/Mg/AcOH and PVA/AcOH/Mg/AKG) it was found that PVA/AcOH exhibited the highest degree of hydrophilicity with the contact angle of 64.5% ± 2% whereas all samples appeared stable in acidic, neutral and basic conditions ruling out the potential for inflammation and/or disintegration in in-vivo environment. PVA/AcOH and PVA/AcOH/Mg showed a stable swelling rate which would maintain the mechanical stability and function inside the body, while PVA/AcOH and PVA/AcOH/Mg/AKG linearly degraded. Lastly, PVA/Mg/AcOH/AKG displayed high hygroscopicity, next to PVA/Mg/AcOH which was second second-highest. Statistically analysis concluded PVA/Mg/AcOH as the best-suited material for fabrication of wound healing suture films.
Keyword: Wound care, biocompatible films, Revolutionizing, advanced wound healing

Background
Wound closure techniques, such as suturing, have been widely employed for centuries in the field of medicine. However, there is a growing interest in exploring alternative biocompatible and biodegradable materials that can promote effective wound healing. This research article aims to present a novel approach utilizing bio absorbable synthetic or naturally occurring adhesives for wound healing, specifically focusing on the development of wound healing tape/films for tissues that experience continuous stress, such as the esophagus, intestines, and intercostal muscles.

Traditionally, topical and transdermal wound healing mediums, including emulsions, creams, gels, and patches, have been utilized [1, 2, 3]. However, these methods may not provide sufficient

mechanical stability when applied to tissues under constant movement and stress. Therefore, the objective of this study is to fabricate wound healing films that exhibit exceptional sturdiness to withstand mechanical stresses while maintaining their chemical properties. These films should also mimic the body's chemical environment, ensuring biocompatibility, optimum pH maintenance, and gradual biodegradability over time [4].

To achieve these goals, polyvinyl alcohol (PVA) has been selected as the base material for film fabrication. PVA is a biopolymer with remarkable characteristics, including biocompatibility, biodegradability, fiber formability, chemical resistance, moisture absorbency, and swelling, making it ideal for wound healing applications [5]. PVA nanofibers possess non-toxic and biocompatible properties, along with optimal oxygen permeability, enabling wound exudate absorption and tissue regeneration [5, 6]. Moreover, the incorporation of metals with PVA enhances the mechanical properties of the resulting nan fibrous mats, thus facilitating cell regeneration [6, 7].

To further enhance the stability and mechanical strength of the PVA solution, dilute acetic acid is introduced, promoting cross-linking by facilitating hydrogen bonding between PVA and acetic acid ions [8]. This cross-linking strategy ensures the film's integrity during the wound-healing process, providing a stable environment for the subsequent addition of minerals to promote cell proliferation.

Among the minerals, magnesium plays a crucial role in wound healing due to its anti-inflammatory properties and its involvement as a cofactor for enzymes in carbohydrate and lipid metabolism [9].

Another important mineral, alpha ketoglutarate (AKG), serves as a weak acid and an intermediate for the tricarboxylic acid (TCA) cycle, which is vital in various metabolic processes. AKG is known for its cell nutritional value and involvement in amino acid synthesis, promoting proteolysis and facilitating the rejuvenation of damaged tissue [10].

This research article presents a novel approach to wound healing by developing biocompatible and biodegradable films designed for tissues under continuous stress. The utilization of PVA as the base material, along with dilute acetic acid, magnesium, and alpha-ketoglutarate, aims to provide mechanical stability, biocompatibility, and an environment conducive to cell proliferation. Compared to traditional suturing techniques, these films hold the potential to minimize scarring, the combination of these minerals and materials would not only provide a mechanically sturdy base but also promote healing through cell proliferation. Compared to traditional suture techniques, this film would leave less of a scar appearance. The chemical properties of the PVA film, along with magnesium, AKG, and acetic acid.

Method details

Fabrication

Materials

The reagent grade materials including Polyvinyl Alcohol (PVA) powder with molecular weight 89,000-98,000 g/mol is procured from Sigma Aldrich. Manganese (IV) oxide is procured from Daejung. Alpha ketoglutarate and Phosphate Buffer Saline (PBS) tablets were procured from G.M Abbas, a local chemical supplier shop located in Karachi, Pakistan.

Methodology

The PVA and PVA/AcOH/MnO2/AKG films were fabricated using solvent casting method. Firstly, 46 ml of distilled water was measured using a measuring cylinder and poured into a 100ml beaker, the beaker was then placed on a magnetic stirrer with a temperature of 60 ºC, for approximately 4 hours (with 15-minute breaks in between). Next, 4 grams of PVA crystals were weighed using a weighing balance and once the water had reached the optimum temperature of 60 ºC, they were added to the water. In order to maintain the temperature and avoid any fumes from leaking, the beaker was covered with foil with a perforation made. This prepared a 4% PVA solution. The steps were repeated four times to get four different solutions.

Acetic acid was diluted using by carefully taking 0.2 ml of acetic acid with the help of a pipette and 9.8 ml of distilled water. Both were added to a measuring cylinder and a glass rod was used to stir. This prepared a 2% acetic acid.

Magnesium and alpha-ketoglutarate tablets were crushed using a mortar and pestle to get a homogenous powder form of both.

Four separate samples were made with the first one being a pure PVA mixture as prepared, this was considered as the control group of the experiment. In the other 3 PVA solutions, 2ml of the dilute acetic acid each was added using a pipette. In the third and fourth samples, 2 mg of Magnesium was added. Lastly, in the fourth solution, 0.4 mg of alpha-ketoglutarate powder was added. Measurements were taken from a weighing balance with a precision of ±0.01. As a result, the following 4 samples were prepared:

1. Pure PVA solution
2. PVA + Acetic Acid
3. PVA + Acetic Acid + Magnesium
4. PVA + Acetic Acid + Magnesium + alpha-ketoglutarate

The mixtures were stirred for a few more minutes again to achieve homogeneity. Using a mechanical pipette of 5 ml of each solution was taken and poured on a labeled petri dish. It was ensured that the mixture had spread evenly on the surface of the petri dish which was then placed in a drying oven for approximately 2-3 hours at 50 ºC. It was checked in intervals if the moisture had completely evaporated. Figure 1 represents the steps involved in fabricating the PVA films.

Method validation

The study conducted by Chaouat et al. focuses on the development and evaluation of a cross-linked poly (vinyl alcohol) (PVA) material for vascular grafts [11]. The authors investigate the cross-linked PVA's mechanical properties, biocompatibility, and degradation behavior. Their findings suggest that the material exhibits favorable mechanical properties, good biocompatibility, and controlled degradation, making it a promising candidate for vascular graft applications. Further research and in vivo studies are needed to validate its performance.

Water Contact Angle

A 2µL drop was placed on three samples of each of the films and a combination of video and photos was used to capture and upload on ImageJ software where contact angles were measured using the Drop Shape Analysis tool.

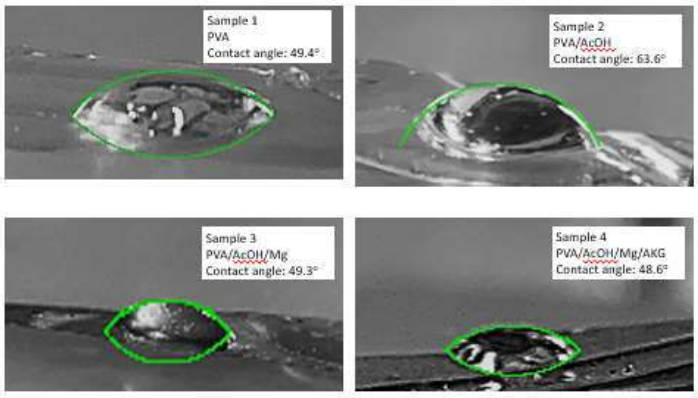


Fig.1: Contact angle contour and measurement

Sample	Constituents	Contact Angle
1	PVA	49.432º
2	PVA/AcOH	63.625º
3	PVA/Mg/AcOH	49.277º
4	PVA/AcOH/Mg/AKG	48.662º

Table 1: Contact angle of each sample

The average contact angle across all four samples was measured to be 52.75 degrees, which aligns with the optimal level of hydrophilicity reported in existing literature. However, the sample with PVA/AcOH displayed a deviation from this mean, exhibiting higher hydrophilicity compared to the other films.

Swelling and Degradation Ratio

The swelling test results are crucial for evaluating the application of the fabricated suture wounds. PVA/AcOH/Mg/AKG displayed the highest fluid absorption, which renders it unsuitable for in vitro wounds due to the potential for promoting infections and microbial proliferation around the healing site. Moreover, excessive fluid retention may hinder the healing process by preventing a drying environment necessary to avoid hydrolysis of protein structures' cross-linkages [12].

Initially, three films were cut from each of the four samples, each measuring 1x5cm. The purpose was to maintain consistency and eliminate any irregularities. The weight of each film was recorded before immersing them in a 5ml Phosphate-buffered Saline (PBS) solution with a pH of 7.38. After 15 minutes, the first measurement was taken by placing each film on a dry filter paper to remove excess fluid, then weighing them using a precision balance with a readability of 0.001 g. This process was repeated at regular intervals of 15 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 5 hours, and up to 16 days. The mean value was calculated for each sample, and any abnormal readings were excluded. After 12 days, the films were discarded, and a fresh PBS solution was used. The obtained measurements were used with a formula derived from literature to determine the swelling degree and degradation [13].

$$Esw = \frac{Wsw - Wo}{Wo} \times 100$$

Where W_{sw} represents the swelling ratio at various time intervals whereas W_o is the initial weight of sample.

These values were then used to create a graph, with the time period scaled to hours on the x-axis and the weight changes represented on the y-axis.

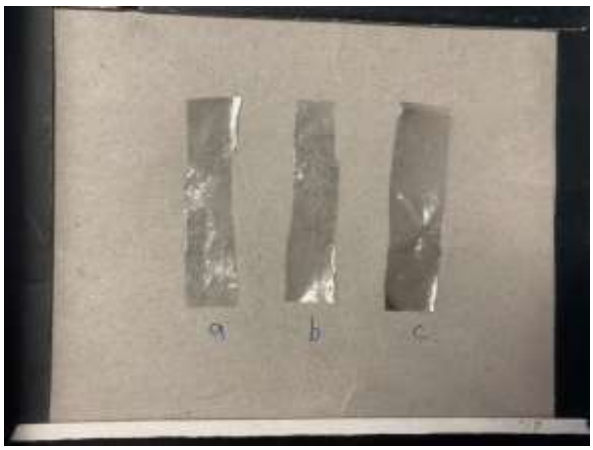


Fig. 2: 1x5cm specimen of each sample

Fig. 3: samples immersed in PBS

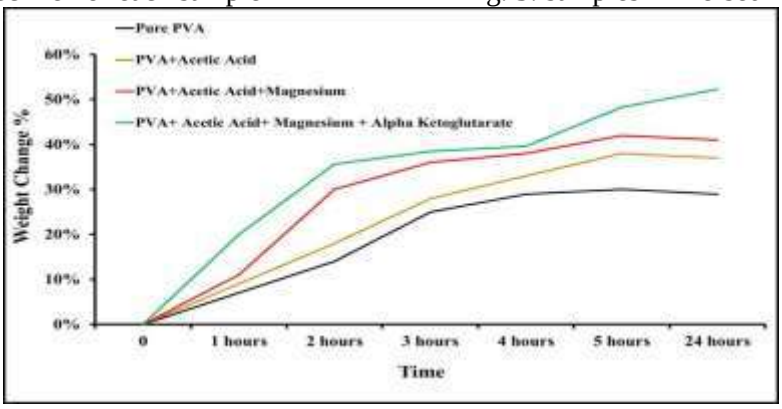


Fig. 4: Rate of Swelling

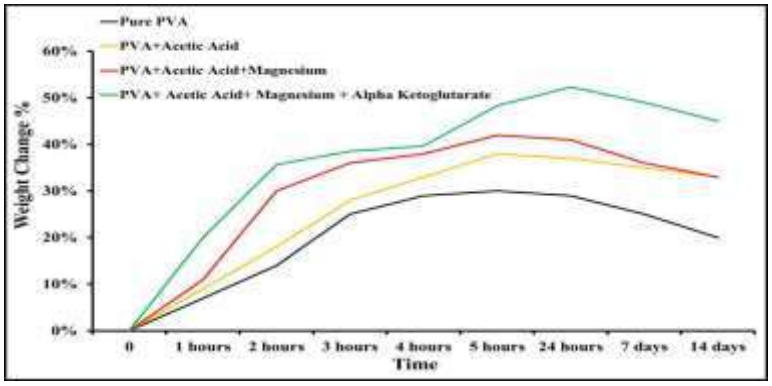


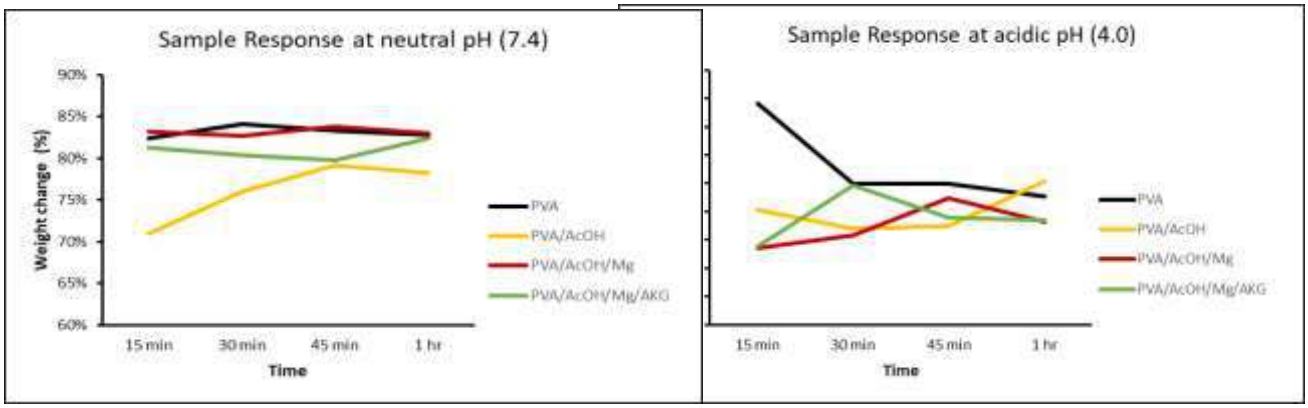
Fig. 5: Rate of Degradation

Based on the graph analysis, it can be inferred that the samples achieved their maximum weights after undergoing swelling, with PVA/AcOH/Mg/AKG exhibiting the highest degree of swelling by

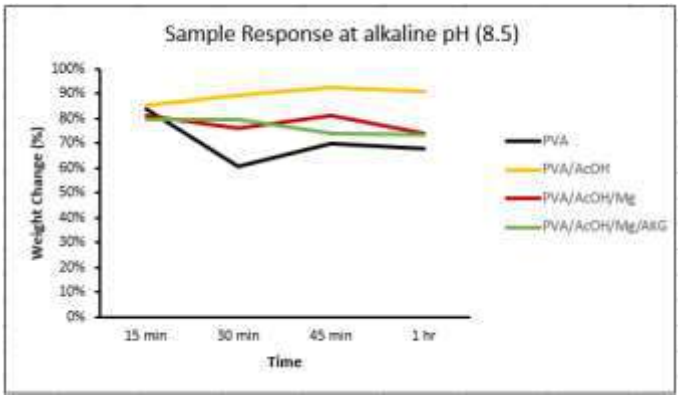
absorbing the greatest amount of water, while PVA/AcOH/Mg showed the least absorption of the PBS solution. Subsequently, all samples began to degrade after reaching the peak swelling point. PVA/AcOH/Mg/AKG experienced a sharp decline in weight, indicating significant degradation, whereas samples 2, 3, and 4 maintained their weights relatively stable. However, the control sample (PVA) deviated from this trend, as its weight initially decreased slightly and then increased before dropping again. Another peak in swelling was observed shortly after the 12-day period when the PBS solution was changed, followed by a similar pattern of degradation.

pH test

It can be proven from the literature that different pH levels can alter the mechanical tensile strength of a polymer [14]. Three solutions of varying pH were produced by adding acid and base to neutral PBS solution. Each of the samples were placed in 3 solution of pH 4, 7.4 and 8 corresponding to various internal body environments. The samples were weighed before immersion and at regular intervals of 15 minutes for a few hours. The percentage of weight gain/loss were recorded.



a **b**



c

Fig. 6: Weight changes in different pH solutions (a) neutral, (b) acidic, (c) basic

Conclusion

It is inferred from the test findings that Sample 3, which comprises PVA, acetic acid, and magnesium, is the best formulation for the suture tape. This material showed improved degrading characteristics,

reduced swelling, and optimal hydrophilicity. These qualities are especially beneficial because they promote efficient wound healing by preserving a suitable moisture balance and guaranteeing prompt material biodegradation.

Limitations

The importance of in vivo and in vitro studies cannot be overstated, as they serve as crucial stepping stones in translating research findings into practical applications. In vivo studies allow researchers to evaluate the behavior of materials within living organisms, providing insights into their biocompatibility, potential side effects, and overall performance. These studies enable the identification of any potential complications or challenges that may arise during real-life applications. On the other hand, in vitro studies provide controlled environments where specific aspects of a material's behavior, such as cell interaction and cytotoxicity, can be thoroughly examined.

The findings from in vitro tests contribute to the development of new biomaterials and medical devices, benefiting industries such as biomedical engineering, regenerative medicine, and healthcare. In the case of Alexandre et al.'s study, the promising results of PVA hydrogel's biocompatibility and hemocompatibility make it a potential candidate for vascular grafting applications [15]. The ability to replace or repair damaged blood vessels using biocompatible materials can significantly impact the field of vascular surgery, improving patient outcomes and quality of life. Additionally, these findings can guide further research and development in the design and optimization of vascular graft materials, leading to advancements in other areas of medical device manufacturing and tissue engineering.

References

[1] *Nussinovitch, A., Gal, A., Padula, C., & Santi, P. (2008). Physical characterization of a new skin bioadhesive film. AAPS PharmSciTech, 9, 458-463.*

[2] *M. Dittgen, Transdermal therapeutic systems (TTS), Med. Monatsschr. Pharm. 21 (12) (1998) 366–377.*

[3] *S. Venkatraman, R. Gale, Skin adhesives and skin adhesion: 1. Transdermal drug delivery systems, Biomaterials 19 (13) (1998) 1119–1136.*

[4] *K. Kim, H. Lee, S. Hong, TAPE: A biodegradable hemostatic glue inspired by a ubiquitous compound in plants for surgical application, J. Vis. Exp. (112) (2016) e53930.*

[5] *A.W. Jatoi, H. Ogasawara, I.S. Kim, Q.Q. Ni, Polyvinyl alcohol nanofiber based three phase wound dressings for sustained wound healing applications, Mater. Lett. 241 (2019) 168–171.*

[6] *R. Ahmed, M. Tariq, I. Ali, R. Asghar, P.N. Khanam, R. Augustine, A. Hasan, Novel electrospun chitosan/polyvinyl alcohol/zinc oxide nanofibrous mats with antibacterial and antioxidant properties for diabetic wound healing, Int. J. Biol. Macromol. 120 (2018) 385–393.*

[7] *K. Kalantari, E. Mostafavi, B. Saleh, P. Soltantabar, T.J. Webster, Chitosan/PVA hydrogels incorporated with green synthesized cerium oxide nanoparticles for wound healing applications, Eur. Polym. J. 134 (2020) 109853.*

[8] *T. Mohamood, F. Al-Zahara, N. Zainuddin, S.W. Tan, Preparation, optimization and swelling study of carboxymethyl sago starch (CMSS)–acid hydrogel, Chem. Cent. J. 12 (1) (2018) 1–10.*

[9] H. Afzali, A.H. Jafari Kashi, M. Momen-Heravi, R. Razzaghi, E. Amirani, F. Bahmani, H.R. Gilasi, Z. Asemi, The effects of magnesium and vitamin E co-supplementation on wound healing and metabolic status in patients with diabetic foot ulcer: A randomized, double-blind, placebo-controlled trial, Wound Repair Regen. 27 (3) (2019) 277–284.

[10] F. Legendre, A. MacLean, V.P. Appanna, V.D. Appanna, Biochemical pathways to α-ketoglutarate, a multi-faceted metabolite, World J. Microbiol. Biotechnol. 36 (2020) 1–11.

[11]M. Chaouat, C. Le Visage, W.E. Baille, B. Escoubet, F. Chaubet, M.A. Mateescu, D. Letourneur, A novel cross-linked poly(vinyl alcohol) (PVA) for vascular grafts, Biomaterials 23 (23) (2002) 4519–4526, doi:10.1016/s0142-9612(02)00219-9.

[12] M.N. Pervez, G.K. Stylios, Investigating the synthesis and characterization of a novel 'Green' H2O2-Assisted, water-soluble chitosan/polyvinyl alcohol nanofiber for environmental end uses, Nanomaterials 8 (6) (2018) 395, doi:10.3390/nano8060395.

[13]T. Khana, E.H. Mirzaa, N.J. Kurda, M. Naushada, M.U. Haqueb, Fabrication and in vitro evaluation of polyvinyl alcohol/bio-glass composite for potential wound healing applications.

[14]E. Chung, N. McPherson, A. Grant, Tensile strength of absorbable suture materials: In vitro analysis of the effects of pH and bacteria, J. Surg. Educ. 66 (4) (2009) 208–211.

[15]N. Alexandre, J. Ribeiro, A. Gartner, T. Pereira, I. Amorim, J. Fragoso, A. Lopes, J. Fernandes, E. Costa, A. Santos-Silva, M. Rodrigues, J.D. Santos, A.C. Mauricio, A.L. Luís, Biocompatibility and hemocompatibility of polyvinyl alcohol hydrogel used for vascular grafting—In vitro and in vivo studies, J. Biomed. Mater. Res. A 106 (5) (2018) 1259–1270, doi:10.1002/jbm.a.36392.