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RESEARCH ARTICLE

Formulation Development and Evaluation of Film Liquid Bandage Using Gallic Acid for Wound Healing

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Abstract

Background: Wound healing is a complex process requiring optimal tissue repair and regeneration conditions. Liquid bandages (L-bandages) offer an innovative approach to wound care by forming a protective film over wounds, aiding healing and preventing infections. Gallic Acid (GA), known for its anti-inflammatory, antibacterial, and antioxidant properties, is a promising natural agent for wound healing. **Aim:** This study aims to develop and evaluate a film-forming L- bandage incorporating GA for effective wound healing. **Methods:** Various formulations were prepared using film-forming agents such as xanthan gum, pectin gum and polyvinyl pyrrolidone, with GA as the active ingredient. The formulations were evaluated for physical properties, including pH, viscosity, drying time and film characteristics such as flexibility, washability, and stickiness. *In vitro* studies were conducted to assess skin permeation and drug retention. **Results:** The optimised formulation demonstrated desirable physical properties, including a pH of 5.6, appropriate viscosity and rapid drying time. The film was flexible, easily washable and exhibited minimal stickiness. *In vitro* permeation studies showed effective skin penetration and retention of GA, indicating its potential for sustained therapeutic action. **Conclusion:** The GA-based L- bandage showed promising results as a wound healing agent, offering a natural, effective solution for protecting and treating superficial skin injuries. The formulation's favourable physical properties and drug delivery potential support its use as an innovative wound care product. Further studies are warranted to confirm its efficacy in clinical settings.

Keywords: Gallic Acid, *In Vitro* Skin Permeation, Liquid-Bandage, Retention Study and Wound Healing

1. Introduction

A wound, defined as damage to biological tissue encompassing the skin, mucous membranes or internal organ tissues, undergoes a complex restorative process known as wound healing[1]. This intricate journey involves stages such as hemostasis, inflammation, proliferation and tissue remodelling or resolution. Wounds, varying in severity based on factors like source, location and depth, prompt two distinct processes: healing and regeneration[2]. While healing often restores early structures, regeneration aims for tissue restitution without scarring through collagen deposition[3].

Crucial to this healing cascade are Reactive Oxygen Species (ROS), including hydrogen peroxide (H_2O_2) and superoxide (O_2), acting as cellular messengers[4]. These ROS activate fundamental wound healing

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processes like cell motility, cytokine action and angiogenesis[5]. However, an ROS level imbalance induced by factors such as hypoxia or hyperoxia can exacerbate tissue damage. Traditional practices involve herbal remedies to create an optimal natural healing environment, cleansing wounds, removing dead tissue and fostering moisture.

In the realm of wound closure, film-forming solutions or gels, whether natural like fibrin or synthetic like cyanoacrylates, serve as tissue glues[6]. The selection of polymers plays a crucial role in crafting effective wound dressings, with synthetic polymers often cross-linked with natural counterparts for enhanced mechanical performance. An innovative approach introduces L- bandages as an alternative to traditional wound care methods, offering a semi-transparent adhesive substance sprayed or painted directly onto wounds. These L-bandages create a protective polymer film, shielding the wound from infection while maintaining a proper moisture balance, thereby promoting skin wound healing.

A breakthrough in L-bandage formulation incorporates GA, a tri-phenolic molecule renowned for its anti-inflammatory, antibacterial and antioxidant properties. GA extends its pharmacological prowess to include anti-tumour, anti-diabetes and anti-obesity actions. The development of a herbal L- L-bandage featuring GA aims to offer a natural alternative for minor wound care[7]. Comprising essential oils, plant extracts and herbal remedies, these L-bandages harness centuries-old healing knowledge. The incorporation of GA enhances therapeutic benefits, making it an effective solution for promoting wound healing through its antioxidant, antibacterial and anti-inflammatory properties. In essence, the herbal L-bandage aspires to provide a safe, efficient, and natural approach to minor wound care.

2. Materials and Methods

Xanthan gum, pectin gum, guar gum, nitrocellulose, polyvinyl pyrrolidone, ethyl acetate, ethanol, benzyl alcohol, isopropyl myristate, castor oil and GA were procured from Sulab Laboratory, Vadodara.

2.1 Method of Preparation of Liquid Bandage

The method of preparation of film L-bandage using GA for wound healing is shown in Figure 1. The pictorial representation of the preparation of L-bandage is shown in Figure 2.

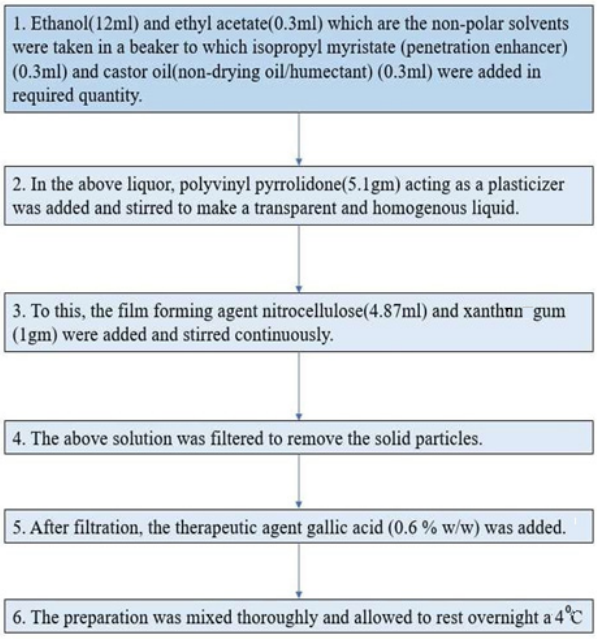


Figure 1. Flow chart of preparation of liquid bandage.

2.2 Development of L-Bandage

Table 1 represents the ingredients present in all the formulations.

2.3 Remarks

Table 2 represents the results for all the batches.

3. Evaluation of Liquid Bandage

3.1 Physical Examination of the Formulation

Various film thicknesses were prepared to facilitate the application of the L-bandage. Under laminar flow conditions, the L-bandage solution was uniformly mixed and poured into clean glass plate moulds of varying thicknesses and kept at room temperature to



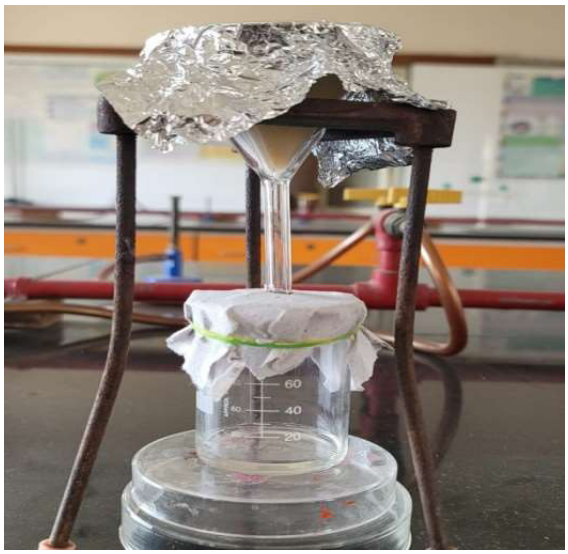
Liquor formation.



The addition of a film-forming agent.



Filtering the solid particles.



Collection and addition of gallic acid.



Pouring the formulation and leaving it overnight in the refrigerator.

Figure 2. Pictorial representation of preparation of L-bandage.

Table 1. Development of L-bandage

Ingredients	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10	B11	B12	B13	B14	B15	B16	B17	B18	B19	B20
Xanthan Gum	2.3gm	-	2.3gm	3gm	-	-	-	1.5gm	-	2.3gm	-	-	-	-	-	-	0.5gm	1.5gm	1gm	1gm
Pectin Gum		2.3 gm			3 gm	3 gm			1.5 gm		2.3 gm	2.3 gm	6 gm							
Guar Gum							2.3 gm													
Nitrocellulose														11.86 ml	11.21 ml	4.87 ml	4.87 ml	4.87 ml	4.87 ml	4.87 ml
Polyvinyl Pyrrolidone	5.1gm	5.1 gm	5.1 gm	5.8 gm	5.8 gm	5.8 gm	5.1 gm	0.15 gm	0.15 gm	5.1 gm	5.1 gm	5.6 gm	5.1 gm	5.1 gm	0.15 gm	5.1 gm	5.1 gm	5.1 gm	5.1 gm	5.1 gm
Ethyl Acetate	7.77 ml	7.77 ml	7.77 ml	8.47 ml	8.47 ml	8.47 ml	7.7 ml	0.3 ml	0.3 ml				0.3 ml	7.7 ml	0.3 ml	0.3 ml	0.3 ml	0.3 ml	0.3 ml	0.3 ml
Ethanol										7.77 ml	7.77 ml	7.77 ml	15 ml			15 ml	15 ml	15 ml	15 ml	12 ml
Benzyl Alcohol	7.77 ml	7.77 ml	7.77 ml	8.47 ml	8.47 ml	8.47 ml	7.77 ml	0.3 ml	0.3 ml				0.3 ml	7.77 ml	0.3 ml	0.3 ml	0.3 ml	0.3 ml	0.3 ml	0.3 ml
Isopropyl Myristate								0.3 ml	0.3 ml				0.3 ml		0.3 ml	0.3 ml	0.3 ml	0.3 ml	0.3 ml	0.3 ml
Castor Oil	0.41 ml	0.41 ml	0.41 ml	1.1 ml	1.1 ml	1.1 ml	0.41 ml	0.03 ml	0.03 ml	0.41 ml	0.41 ml	0.41 ml	0.3 ml	0.41	0.24 gm	0.3 ml	0.3 ml	0.3 ml	0.3 ml	0.3 ml
Gallic Acid														0.24 gm	0.24 gm	0.24 gm	0.24 gm	0.24 gm	0.24 gm	0.24 gm
FILM FORMED OR NOT?	N	N	N	N	N	N	N	N	N	N	N	N	N	Y	Y	Y	Y	Y	Y	Y

Table 2. Outcomes of all the batches

B-1	No film formation and consistency was too thick.
B-2	No film formation and consistency was too thick.
B-3	No film formation and consistency was too thick.
B-4	No film formation and consistency was too thick.
B-5	Pectin did not dissolve well, neither did the film form.
B-6	Pectin was mixed in water before mixing but it formed mucilage and no film was formed.
B-7	Guar gum did not mix well and no film was formed.
B-8	The solution was less viscous and no film was formed.
B-9	The solution was less viscous and no film was formed.
B-10	Film was formed but Xanthan gum dissolved well and filtered easily.
B-11	Film did not form and the solution was less viscous.
B-12	Film did not form and the solution's consistency improved a little.
B-13	The film formed was gritty, the colour was not proper due to the presence of pectin and the formulation was not viscous at all.
B-14	The film formed was very thin and took a lot of time to dry.
B-15	The film was partly formed and the formulation was not viscous.
B-16	The film formed was thin but took a lot of time to dry and the formulation was not viscous.
B-17	The film formed was fine but the formulation was not visible in the photographs of the body.
B-18	The film formed was thick and took a lot of time and formulation became very thick.
B-19	The film formed was fine drying time decreased a little and consistency was just fine.
B-20	The film formed was nice, dried faster than others and consistency was fine.

evaporate the solvent. The film formed was carefully removed and measured immediately[8].

3.2 Observation of the Film Formed Under a Different Microscope

The film formed was viewed under a microscope to observe the structure of the film with the help of a microscope (scanning electron microscope)[9].

3.3 PH of the Formulation

To increase the stability of the active ingredient and adapt it better for the intended application, its pH value was tested and modified. A pH of 4-6 is thought to be optimum for skin, diabetic wounds have a pH range of 6.5–8, while burns heal more quickly at pH 7.32. The preparation's pH was changed to avoid irritation and modifications to the wound's physiological state while it heals. Furthermore, depending on the dosage's pH value, the degree of ionisation may also have an impact on how much of the medication penetrates the skin. The pH of the L-bandage formulation was measured with a digital pH meter. Three copies of the measurement were made and an average was calculated[9].

3.4 Drying Time of the Film/ Film Forming Time

To find out how soon the film developed after the solution was applied, the drying time of the film was measured. The solution may be applied to the glass surface and left to dry at room temperature, depending on the circumstances. Applying a film-forming solution to the skin allows for direct observation of the drying process. The film is placed without pressing it on a glass plate to see if it has dried. If there is no adhesion between the film and the glass, the film is said to be dry. Since the drying duration for this test may differ from that of the glass plate test, it is more typical of real-world settings because the skin has pores and body heat. Drying time was calculated by using a stopwatch. Following the application of the formulation to the glass plate, the watch was started and stopped when the solvent or film had completely evaporated or dried[8].

3.5 Determination of Viscosity

Depending on its kind and concentration, the former agent in the film will have a different viscosity. Since the film-forming solution's viscosity will affect how easily it spreads, it is crucial to take this into account. By raising the film-forming solution's concentration, the coverage can be decreased. Using a Brookfield Viscometer, model DV-||+pro, the formulation's viscosity was determined at 10, 20, 50 and 100rpm. After dipping the spindle in the formulation for roughly five minutes in a beaker, the reading was obtained[8].

3.6 Moisture Content

By comparing the initial weight of the film (W1) with the weight of the film after one day of storage (W2), the film's moisture content was assessed. The following equations can be used to calculate moisture loss and moisture uptake[5].

Moisture loss (%) = W1-W2/W1 × 100%

Moisture uptake (%) = W2-W1/W2 × 100%

3.7 Film Occlusion Potential or Water Vapour Permeability

Determining the film's permeability to wound fluid is crucial as well, as it influences the wound's moisture content. Infection-causing microorganisms can flourish in conditions of extreme humidity.

50 mL of water was added to a glass beaker that had filter paper covering it for this test. One of the papers was sprayed with a film-forming solution to create a film. The beaker was then kept in storage at normal temperature and humidity levels. The beaker's decreased water weight was used to calculate the film's water permeability. This formula was used to determine the assessment.

F = A-B/A × 100

Where,

F = The occlusivity factor

A = The reduction in water weight in the glass beaker covered with filter paper without a film.

B = Water weight reduction when the filter paper is coated with the film in the glass beaker.

The smaller the occlusivity factor value, the better the film permeability.

3.8 Stickiness

Cotton wool was used to gently press the dried film. The viscosity of the film was ascertained by counting the number of cotton wool fibres affixed to it. Adhesiveness of a film is classified as high if its fibres are dense, medium if they are thin and low if none or very few are attached. It must be examined while being moved since stickiness is also evaluated to see if the film would easily attach to clothes or other items[10].

3.9 Demonstration of Excellent Tissue Adhesion of the L-bandage

3.9.1 Adhesion Behaviour of the Formulation

Adhesion behaviour was witnessed by applying the formulation on the slide and covering it with another slide to observe its structure network.

3.9.2 Adhesion to Joint

In actual use, the joint is difficult to stick to and is prone to falling off. Consequently, there is a great need to increase the wound bandage's ability to adhere. As a result, the L-bandage was applied to the finger joints. It demonstrated its excellent adaptation and adherence by sticking securely to the skin even as the fingers bent and extended repeatedly[9].

3.10 Water Washability

In the dried film, the film's wetting ease was evaluated. Water was used to wash the film, and its evaluation was done on an ordinal scale: easily, somewhat and poorly. If the film-forming solution comes into touch with delicate body parts like the mouth or eyes, having an easily washable solution could be beneficial[11].

3.11 Film Flexibility

Stretching the skin in two or three directions allowed us to measure skin fixation, which was used to assess the flexibility of the film. If there is neither skin fixation nor cracking, the film is classified as non-flexible; if both, it is rated flexible[12].

3.12 Characterisation by FTIR

Characteristic Infrared Spectroscopy (IR) peaks identified the chemical structure of nitrocellulose-xanthan gum films containing GA. Fourier Transform Infrared Spectroscopy (FTIR) was performed for the L-bandage and GA formulation with the Bruker Platinum-ATR Alpha-II IR spectrometer. Infrared analysis was performed with a spectral range of 4000-400cm^{-1} with 2cm^{-1} resolution[13].

3.13 *In Vitro* Permeation Study

Predicting the properties of drug penetration *in vivo* is done using *in vitro* diffusion experiments. The drug's release profile from the film-forming mechanism is ascertained using the Franz diffusion cell. The diffusion membrane is linked between the two compartments that make up the cell: the donor and the recipient compartments. The receptor compartment holds the diffusion medium, while the donor compartment is open to the environment. Samples can be taken with the help of the receptor compartment's sampling arm. The donor compartment is coated with a preset amount of the drug-containing film-forming formulation. Samples are gathered and subjected to an appropriate spectroscopic technique for drug release analysis. Here, the goat skin was taken to perform the study. The hair was removed from its superficial skin layer and the subcutaneous fat was carefully dissected with surgical scissors. A skin piece of 2x2cm was cut and attached to the diffusion cell, which acted as the diffusion membrane. The phosphate buffer (pH 7.2) was used as a diffusion medium in the receptor compartment. A predetermined quantity of the formulation containing the drug was placed in the donor compartment and the assembly was kept on the magnetic stirrer (rpm 50). Samples were collected at a regular time interval of 30 minutes and analysed by Ultraviolet (UV)-spectrophotometer for drug release[14].

3.14 Skin Retention Study

In vitro diffusion experiments are used to predict how effectively drugs would permeate biological organisms. The Franz diffusion cell measures the medication's release profile from the film-forming equipment. The diffusion membrane, which can be a cellophane or egg membrane, connects the cell's two compartments, the donor and the recipient compartment. The diffusion medium is inside the receptor compartment, leaving the donor compartment open to the atmosphere. Sampling is enabled via the sampling arm of the receptor compartment. A preset amount of the drug-containing film-forming formulation is applied to the donor compartment. Spectrophotometric methods that are appropriate for drug release are used to collect and analyse samples[15].

4. Results and Discussion

4.1 Physical Examination of the L-bandage

A physical evaluation was carried out for the bandage. Results are shown in Table 3.

Table 3. Observation of physical parameters of formulation

Parameter	Observation
Homogeneity	Clear, transparent solution with no suspended solid particles.
Colour	Sunset Yellow
Consistency	Slightly viscous.
Odour	Ether-like (mildly pungent)

4.2 Thickness of the Formed Film

The thickness of the formed film was found to be 0.1mm.

4.3 Observation of Formed Film Under Microscope

The optical microscopy of the film is shown in Figure 3.



Figure 3. Optical microscopy of the formed film.

4.4 pH of the Formulation

The average pH of the final formulation after incorporating the GA was found to be 5.6 which relates to the optimum pH required for the topical skin formulations.

4.5 Drying Time/Film Forming Time

The drying time of the film was found to be 55 seconds on a glass slide. However, it was observed if a single swatch was done it took less time compared to double switching. Double swatch would give more sealant and protective action compared to single. Drying time showed a decrease when ethanol concentration was decreased. However, below a certain limit, the film does form but starts cracking as soon as it gets dried, concluding that the concentration of the solvent should be optimum for the film to retain on the skin.

4.6 Determination of Viscosity

The viscosity of the formulation was noted as above. The viscosity increases with an increase in concentration of the film-forming agent like gums.

4.7 Moisture Content

The moisture content of the formulation was found to be 1.9%. It falls within the limits justifying that formulation will have good stability on storage.

4.8 Occlusion Potential or Water Vapour Permeability

The perfect wound dressing should have several features, including the capacity to regulate the diffusion of gases, the ability to keep the surrounding area wet, the ability to stop more inflammation, ease of use with minimal discomfort from the wound, cosmetic acceptability and affordability. For the films to aid in wound healing, they must be permeable to regulate gases and moisture. The ideal value for wound healing was found to be 20.11 for the water vapour permeability or occlusion potential.

$F=A-B/A*100$

A=1.69gm (decrease in water weight in the glass beaker covered with filter paper without a film.)

B=1.35gm (reduction in water weight in the glass beaker covered with filter paper coated by the film.)

$F=1.69^{-1}.35/1.69*100$

$=20.11$

The occlusion potential i.e., F was found to be 20.1.

4.9. Stickiness

It was observed that very few fibres of cotton stuck to the film concluding that on the application of the film, it would not adhere to the clothes and hence would not require attention on the move.

4.10 Excellent Tissue Adhesion of L-bandage

The bandage on application to the joint's surface did not undergo breakage and remained intact even on movement of that joint.

4.11 Water Washability

The formulation after the formation of the film was moderately washable with water, which indicates that in case of contact with the formulation, sensitive areas like eyes can be removed (Figures 4 and 5).



Figure 4. Water washability by running tap water.



Figure 5. Water washability under a sprinkling of water.

4.12 Film Flexibility

The formed film was flexible because there were no cracks developed on it on stretching (Figures 6 and 7).



Figure 6. Stretching of the skin in directions after application of the film.



Figure 7. Film intactness after stretching in different directions showcasing the film's flexibility.

4.13 Characterisation by FTIR

IR spectra of GA and the formulation are shown in Figures 8 and 9.

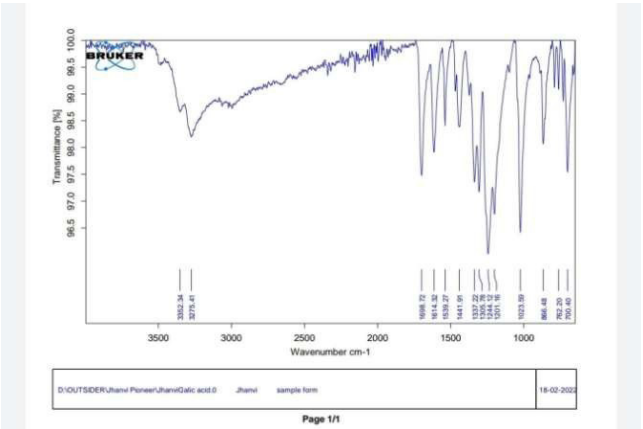


Figure 8. IR spectra of gallic acid.

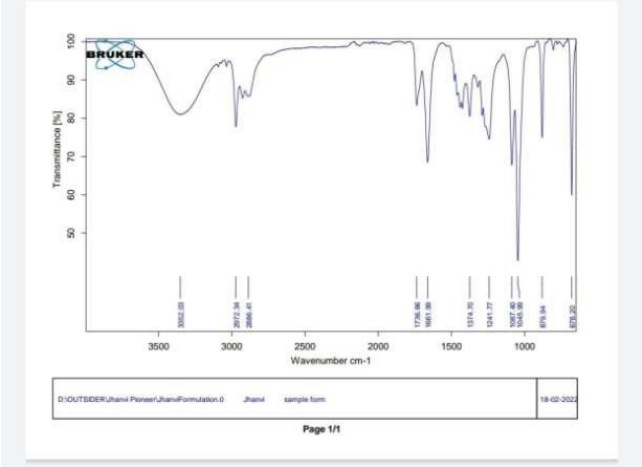


Figure 9. IR spectra of the formulation.

4.14 *In Vitro* Permeation Study

Franz diffusion cell was used to perform the *in vitro* permeation of L-bandage. Phosphate buffer H7.2 was used as a diffusion medium. Figures (10 and 11) show a graphical representation of the permeation of the drug in the diffusion medium at intervals of 30 minutes. For the initial 60 minutes, the release was very low but it increased after that indicating a delayed release i.e., the release of the drug at a time other than immediately.

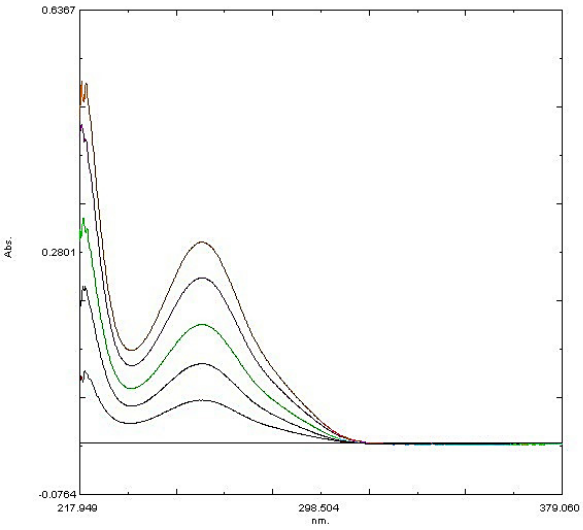


Figure10. UV-spectra of the standard gallic acid calibration curve.

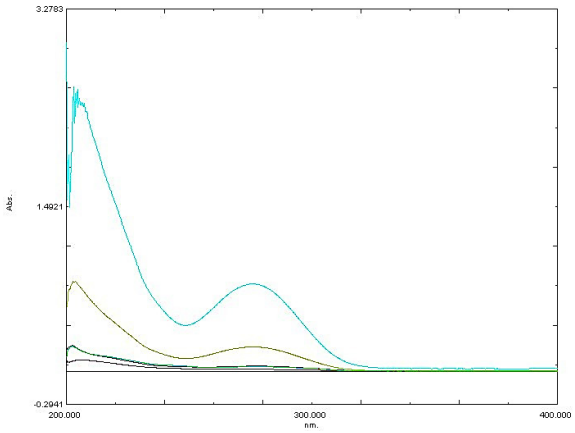


Figure 11. UV-spectra of *in vitro* permeation study of L-bandage containing gallic acid.

4.15 Skin Retention Study

After the *in vitro* study of permeation, the goat skin was taken. The excess formulation was removed and washed in distilled water. The skin was cut into small pieces and vortexed and sonicated with buffer solution and later after filtering the solution, it was diluted and observed under UV. The result of absorbance of this sample solution that was retained in the skin was compared with the standard absorbance of formulation that was first applied on the skin during *in vitro* study. Figure 12 shows a graphical representation of how much drug was instilled via the standard formulation compared to how much drug was retained in the skin at the end of the study in terms of absorbance (Figure 13).



Figure 12. Minced pieces of goatskin for retention studies.

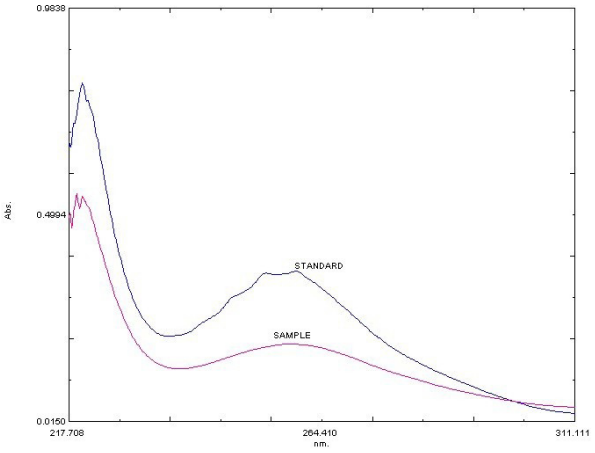


Figure13. UV-spectra of skin retention of drug in comparison to the standard.

4.16 Scanning Electron Microscopy (SEM)

SEM images of the optimised formulation are shown in Figure 14.

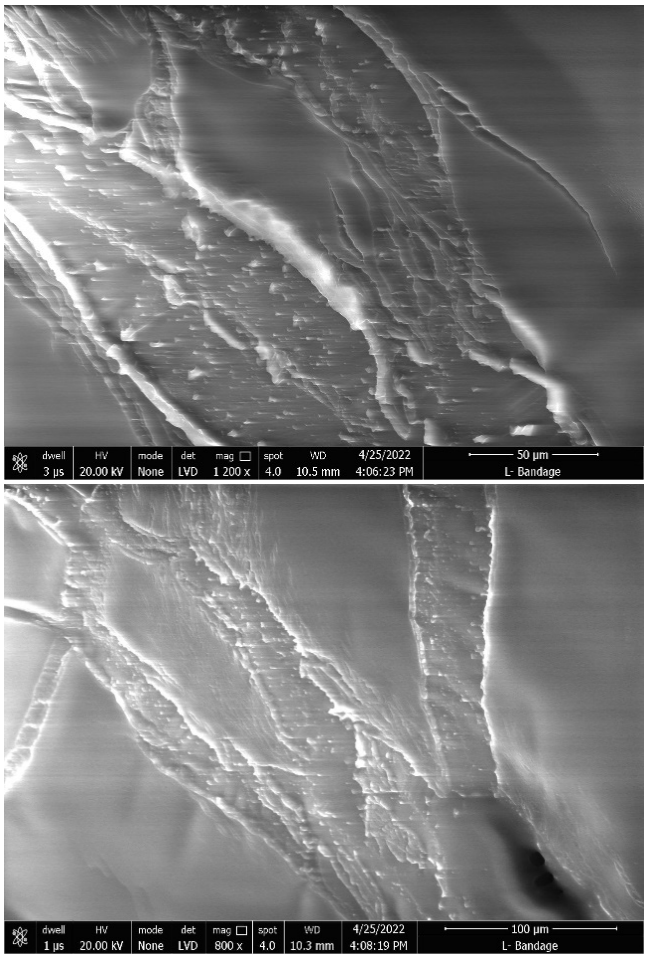


Figure 14. SEM images of the optimised formulation.

5. Discussion

Among the formulated batches, seven batches B14 to B20 were chosen based on film formation capacity and GA incorporation. Physical appearance, viscosity, pH and moisture content were assessed. Film properties such as structure, flexibility, adhesion, washability and occlusion potential were examined. *In vitro* studies evaluated skin permeation and retention of the drug for only the B20 batch was performed. Optimum results were obtained, complying with topical preparation requirements. The GA release showed delayed drug release, while the skin retention study indicated significant drug concentration on the skin. The developed L-bandage exhibited promising wound-healing properties, making it a novel option for small cuts, bruises and abrasions.

6. Conclusion

L-bandages, a film-forming system, offer innovative drug delivery to the skin, providing advantages like transparency, non-greasiness and improved patient compliance. GA, combined with Xanthan gum and nitrocellulose, shows potential for wound healing. *In vitro* studies demonstrate drug permeation and retention in the skin, indicating the L-bandage's efficacy. More research is needed to understand its delivery efficiency, but the results thus far are promising, supporting further development of this novel drug delivery technology.

7. Acknowledgements

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