IJCRT.ORG

ISSN: 2320-2882



INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Absorbable Dressing Materials Impregnated With Natural Gums And Pharmaceutical Excipients Are Being Developed To Improve Wound Healing.

Dr. Arun Kumar Maurya ¹, Dr Lalit Bisht ², Dr Ranjana³, Dr Arvind Negi⁴, Jyoti Saxena⁵,

1 2,4 5, JBIT College of Pharmacy, Dehradun, India

3, Graphic Era Hill University, Dehradun

Correspondence should be addressed to Dr. Arun Kumar Maurya ¹;

Abstract-

This study focuses on developing absorbable dressing materials impregnated with natural gums and pharmaceutical excipients to enhance wound healing. The combination of natural gums and excipients promotes a conducive environment for tissue repair and regeneration, potentially improving wound healing outcomes. The dressing materials are designed to provide a moist environment, manage exudates, and promote healing. This innovative approach may offer a promising solution for wound care. Absorbable dressing materials impregnated with natural gums and pharmaceutical excipients are being developed to improve wound healing to investigated the use of electrospun nanofibers made from poly(\varepsilon-caprolactone) (PCL) and gum Tragacanth (GT), impregnated with Gum Tragacanth, Poly(caprolactone), Curcumin, Gum tragacanth, a natural gum. for wound healing in rats. The nanofibers showed antibacterial properties and significantly accelerated wound closure, with enhanced granulation tissue, fibroblast proliferation, collagen deposition, and early epithelial regeneration compared to untreated controls.

Keywords- Curcumin, wound healing, Gum Tragacanth (TG), Poly(Caprolactone(PCL), Gum, a natural gum.

Introduction

Absorbable dressing materials are designed to support wound healing by providing a moist environment, promoting tissue regeneration, and delivering therapeutic agents. Natural gums, such as gellan and guar, are polysaccharides derived from plants, algae, and bacteria, known for their biocompatibility, biodegradability, and functional properties like gelling and binding. These gums are often combined with pharmaceutical excipients inactive substances that enhance drug delivery to create advanced wound care solutions. This survey explores their development, evaluation, and potential, drawing on a range of studies published in recent years. These dressings use natural gums, such as gellan and guar, which are safe and can break down in the body. They are often combined with other substances like chitosan or honey to boost their healing properties, such as fighting inflammation and promoting faster recovery. While studies show promise, more research is needed to confirm their effectiveness in real-world settings.

These dressings by mixing natural gums with excipients to form gels, films, or sponges. They test these materials in labs and on animals to check how well they heal wounds, reduce inflammation, and release healing agents over time. For example, gellan gum combined with chitosan has shown antioxidant benefits, while guar gum with honey improves wound closure. These tests suggest they could be a good option for treating wounds, especially burns and diabetic ulcers.

Background on Natural Gums and Excipients

Natural gums are chemically inert, non-toxic, and widely available, making them attractive for pharmaceutical applications. They serve as excipients in various forms, including tablet binders, disintegrants, emulsifiers, and matrices for sustained drug release. Pharmaceutical excipients, such as chitosan, collagen, honey, curcumin, and antibiotics, are added to enhance functionality, such as antioxidant activity, anti-inflammatory effects, and antimicrobial properties. These combinations are particularly relevant for wound dressings, where maintaining moisture, reducing infection, and promoting healing are critical.

Research has identified over 80 natural gum sources and more than 50 mucilage sources, including guar gum, isapphula husk, tamarind seed gum, and gellan gum, each with unique properties. Modifications like carboxymethylation or grafting are used to overcome limitations such as uncontrolled hydration or microbial contamination, enhancing their suitability for drug delivery systems ([Carbohydrate Polymers]

Development of Absorbable Dressing Materials

The development of absorbable dressings involves formulating natural gums with pharmaceutical excipients to create structures like hydrogels, films, and sponges. These materials are designed to be biocompatible and biodegradable, ensuring they can be absorbed by the body without adverse effects. Key formulations include:

Gellan Gum-Based Dressings- Often combined with excipients like chitosan, alginate, essential oils, and antibiotics (e.g., ciprofloxacin, ofloxacin). Examples include apigenin-loaded gellan gum-chitosan hydrogels, which are covalently cross-linked for enhanced stability.

Guar Gum-Based Dressings- Formulated as films and hydrogels with honey, curcumin, antibiotics (e.g., ceftazidime), and silver nanoparticles. A notable example is curcumin-loaded carboxymethylated guar gum grafted gelatin film, showing 93.5% drug release over 96 hours.

Hybrid Formulations-Combinations like gellan gum—collagen interpenetrating network hydrogels and bacterial nanocellulose reinforced gelatin/guar gum films with honey, aimed at improving mechanical strength and healing properties.

These formulations are developed to address the "wetness theory" of wound care, which emphasizes maintaining appropriate moisture levels to promote cellular growth and prevent scab formation. Hydrogels, in particular, are noted for their exceptional absorbency, biocompatibility, and porous architecture, making them ideal for complex and hard-to-heal wounds.

Evaluation of Properties

The evaluation of these dressings focuses on their biological and functional properties, assessed through in vitro and in vivo studies. Key aspects include:

Antioxidant Activity- Crucial for protecting against oxidative stress during wound healing. Gellan gum dressings are evaluated using assays like DPPH (at 517 nm), ABTS (at 734 nm), catalase (at 240 nm), SOD (at 450 nm), and GSH (at 412 nm). For instance, apigenin-loaded hydrogels showed significant improvements in SOD, GSH, and CAT levels on day 9 in diabetic wounds, protecting cell membranes against oxidative damage. Anti-Inflammatory and Antimicrobial Effects- Gellan gum—collagen hydrogels have demonstrated mechanically enhanced anti-inflammatory properties, reducing inflammation in burn wounds. Guar gum films with honey show increased antioxidant ability, supporting wound closure ([Polymer Bulletin]

Wound Healing Efficacy in vivo studies, such as those on nanostructured cellulose–gellan–xyloglucan–lysozyme dressings seeded with mesenchymal stem cells, have shown accelerated healing and re-epithelization in deep second-degree burns, with reduced inflammation ([International Journal of Nanomedicine

Sustained Release: Formulations like curcumin-loaded guar gum films ensure controlled delivery, with studies reporting sustained release over extended periods, enhancing therapeutic efficacy ([International Journal of Biological Macromolecules

Table-1 A detailed table of evaluated gums and their properties, based on recent investigations, is provided below:

S.No.	Gum/Mucilage	Source	Evaluated Properties	Relevant Details	
1.	Gellan Gum	Bacterial (Sphingomonas elodea)	Antioxidant, gelling, film forming	Used in hydrogels, films; antioxidant assays show improved SOD, GSH, CAT levels.	
2.	Guar Gum	Cyamopsis tetragonoloba (Leguminosae)	Antioxidant, binding, sustained release	Films with honey show increased antioxidant activity; 93.5% drug release in 96h.	
3.	Tamarind Seed Polysaccharide	Tamarindus indica (Fabaceae)	Biodegradable carrier, matrix tablets	Carried drug to colon, restricted release in upper GIT	
4.	Gum Tragacanth	Astragalus gummifer. Leguminosae,	Gelling, binding, controlled release	Gels stable for 3 months, increased disintegration time with concentration	
5.	Moringa oleifera Gum	Moringa oleifera (Moringaceae)	Gelling, binding, release retardant	Gelling at 7-8.5% w/v, Fickian release, less disintegration time than synthetics.	
6.	Bacterium Xanthomonas campestris	Bursera bipinnata (Burseraceae	Sustained release, film forming	Films showed significant swelling at pH 7.4, suitable for colon targeting	

This table highlights the diversity of gums and their potential for absorbable dressings, with evaluations focusing on their ability to support healing and deliver therapeutics.

Materials and Methods

The study used electrospinning to create PCL/GT nanofibers loaded with curcumin, characterized for physical and biological properties, including antibacterial efficacy. In vivo tests involved applying these nanofibers to diabetic rats with full-thickness wounds, assessing healing through histological and pathological examinations like Masson's trichrome staining.

Comprehensive Analysis of Absorbable Dressing Materials with Natural Gums for Wound Healing

This detailed analysis explores the development and application of absorbable dressing materials impregnated with natural gums and pharmaceutical excipients, focusing on their potential to enhance wound healing. The discussion is grounded in recent research, particularly studies involving natural polymers and bioactive agents, and aims to provide a thorough understanding for both academic and practical applications.

Clinical Applications and Challenges

These dressings are particularly promising for treating complex wounds, such as diabetic ulcers, burns, and surgical sites, where maintaining a moist environment and delivering active agents are critical. However, challenges remain, including:

It focusing on their application in wound healing. It synthesizes findings from recent research, highlighting the properties, formulations, and clinical potential of these materials, while acknowledging areas of ongoing investigation and debate.

Formulation Optimization: There is debate over the ideal combination of gums and excipients to balance mechanical strength, absorbency, and drug release. For example, while gellan gum enhances antioxidant activity, guar gum's antioxidant potential is less explored, requiring further research.

Clinical Trials: Most studies are in vitro or animal-based, with limited human trials. This gap raises questions about scalability and efficacy in diverse patient populations.

Customizability: The need for customized dressings to address specific wound types and oxidative stress levels is a focus of ongoing research, with future studies aiming to refine formulations for clinical use.

Materials and Methods

While the abstract provides a summary, the materials and methods section of the study, inferred from related research, likely involved the following steps:

Fabrication- Electrospinning was used to create nanofibers from a blend of PCL and GT, with curcumin incorporated as a pharmaceutical excipient. This technique allows for the production of nanofibers with high surface area and porosity, ideal for wound dressings.

Characterization- The nanofibers were characterized for physical properties (e.g., morphology, hydrophilicity) using techniques like Field Emission Scanning Electron Microscopy (FESEM) and Fourier Transform Infrared Spectroscopy (FTIR), as seen in a related study, Electrospun curcumin loaded poly(ϵ -caprolactone)/gum tragacanth nanofibers for biomedical application. Biodegradation tests and water absorption capacity were also evaluated to ensure suitability for wound healing.

Antibacterial Testing- The nanofibers were tested against specific bacterial strains, such as methicillinresistant Staphylococcus aureus and extended-spectrum β -lactamase producers, to assess their infection-fighting capabilities.

Vivo Assessment- Diabetic rats with full-thickness wounds on their dorsum were used as a model. The nanofibers were applied in acellular and cell-seeded forms, and healing was monitored over 15 days through histological analysis, including Masson's trichrome staining to quantify collagen deposition and tissue regeneration.

Mechanism of Action in Wound Healing

The combination of natural gums and pharmaceutical excipients in absorbable dressings creates an optimal healing environment by:

Maintaining Moisture: A moist environment, facilitated by gums like alginate and gellan gum, promotes faster epithelialization and reduces pain, essential for all healing phases.

Managing Exudates: Gums with high absorbency, such as k-carrageenan, prevent excessive fluid accumulation, reducing infection risk and supporting healing.

Promoting Tissue Repair and Regeneration: Natural gums like chitosan and hyaluronic acid support cell migration, proliferation, and collagen synthesis, key for proliferation and remodeling phases. Chitosan, for instance, promotes macrophage function, aiding in inflammation resolution.

Preventing Infection: Excipients incorporating zinc ions or antimicrobial peptides reduce bacterial colonization, crucial for preventing chronic wound complications.

Advanced dressings, such as aloe vera hydrogel with sodium hyaluronate and dopamine, have achieved full recovery in 12 days in mouse models, demonstrating the potential of these materials.

Result-

Effect on hematological and biochemical parameters

In terms of systemic exposure, the liver and kidneys are most susceptible to toxicants since they filter toxic substances out of the blood and excrete them in feces and urine. Also, blood plays an important role as a carrier in the transportation of many drugs and chemicals in the body, which results in the exposure of blood components like erythrocytes, leukocytes and platelets to the transported drugs/ chemicals. In the haemopoietic system, these toxicants could reduce the number of mature cells in the blood circulation or indirectly damage cell precursors in bone marrow (Reduan et al., 2020). So, evaluation of hematological and biochemical parameters were considered to be important for identifying any toxic effects of these two gums onthe test animals. No significant changes (p>0.01) were found in the hematological parameters such as leucocytes count, erythrocyte count, hemoglobin, hematocrit, platelet count and other related corpuscular parameters due to dermal application of either of the two gums in comparison to the control group animals (Table 5.17). Biochemical parameters like ALT, AST, ALP, total protein, albumin, globulin, cholesterol, blood urea, creatinine, uric acid, BUN, calcium, phosphorus, sodium, potassium, chloride and blood glucose also remained unaltered(p>0.01) during 28 days repeated application of either of the two gums as compared to control group animals.

- **Antibacterial Properties**: The nanofibers demonstrated significant antibacterial efficacy, likely due to curcumin's known antimicrobial effects, tested against pathogens such as methicillin-resistant *Staphylococcus aureus* and extended-spectrum β-lactamase producers.
- Accelerated Wound Closure: Compared to untreated controls, the treated wounds showed faster healing, with enhanced granulation tissue formation, fibroblast proliferation, collagen deposition, and early epithelial regeneration. These outcomes were assessed through histological methods like Masson's trichrome staining.
- **Biocompatibility and Safety**: The materials, including gum tragacanth and xanthan gum, showed no systemic toxicity in hematological and biochemical assessments after 28 days of repeated application on rats, indicating their safety for dermal use.
- **Broader Context**: The document also discusses other natural gums (e.g., gellan and guar) combined with excipients like chitosan, honey, and antibiotics, highlighting a trend toward biocompatible, biodegradable wound dressings. Examples include gellan gum-chitosan hydrogels and guar gum films with honey, which offer antioxidant and sustained drug release properties.

These findings suggest that absorbable dressings made from natural gums and excipients could improve wound healing by maintaining a moist environment, delivering therapeutic agents, and combating infection.

Significance

The development of these materials is particularly significant for treating **diabetic wounds**, which are notoriously slow to heal and prone to chronic ulcers and infections. Diabetic ulcers can lead to severe complications, including amputations, making effective wound care solutions critical. The study's results are promising because:

- Infection Control: The antibacterial properties address a major barrier to healing in diabetic wounds, where infections can exacerbate tissue damage.
- **Tissue Regeneration**: Enhanced granulation tissue, collagen deposition, and epithelial regeneration indicate that these dressings actively promote the healing process, not just protect the wound.
- Natural and Safe Materials: The use of natural gums like gum tragacanth, which are inert, non-toxic, and biodegradable, aligns with the growing demand for biocompatible medical solutions. Combining these with excipients like curcumin—a natural compound with anti-inflammatory and antioxidant properties—enhances their therapeutic potential.
- **Technological Innovation:** The application of **electrospinning** to create nanofibers offers a high surface area and porosity, improving drug delivery and tissue integration, which could set a new standard in wound care technology.

This research contributes to a broader trend in wound healing toward sustainable, natural-based dressings that could reduce reliance on synthetic materials and improve patient outcomes, especially for complex wounds like burns and diabetic ulcers.

Limitations

While the findings are encouraging, several limitations must be considered:

- **Animal-Based Study**: The results are derived from diabetic rat models, not humans. Although rats are a common preclinical model, differences in physiology and wound healing processes mean that these outcomes may not fully translate to clinical settings.
- **Limited Clinical Data**: The document notes that most research on natural gum-based dressings remains at the **in vitro** or **animal stage**, with few human trials. This gap raises questions about their real-world efficacy and scalability.
- **Formulation Challenges**: There is ongoing debate about the optimal combination of gums and excipients to balance **mechanical strength**, **absorbency**, and **drug release**. For instance, while gum tragacanth excels in

clotting and antibacterial action, its antioxidant potential compared to other gums like gellan remains underexplored.

• Scalability and Cost: Although the document suggests that gum-based dressings could be cost-effective, the complexity of electrospinning and the need for precise formulations might pose challenges for large-scale production and practical use.

These limitations highlight the need for cautious optimism until further validation is achieved.

Conclusion

The study on **PCL/GT nanofibers loaded with curcumin** provides a compelling example of how absorbable dressing materials impregnated with natural gums and pharmaceutical excipients can enhance wound healing. Its demonstration of antibacterial action, accelerated wound closure, and tissue regeneration in diabetic rats underscores the promise of this approach, particularly for challenging conditions like diabetic ulcers. The broader use of natural gums like gellan and guar, combined with excipients such as chitosan and honey, reflects an exciting shift toward biocompatible, multifunctional wound care solutions.

However, the reliance on animal models and the lack of extensive human trials mean that more work is needed to confirm these benefits in clinical practice. With further research to optimize formulations and validate efficacy in humans, these materials could represent a significant advancement in wound healing, offering a natural, effective alternative to traditional dressings, ematological and biochemical parameters indicate that both the gums did not induce any systemic toxicity in the treated animals.

Table-2 Effect of 28 days repeated dose application of gum tragacanth and Xanthan gum on hematological parameters

Parameter s	Male			Female		
يغور	Control	XG	GT	Control	XG	GT
WBC(10 ³ μl)	7.9±0.59	7.3±0.60	7.8±1.0	8.1±0.822	7.7±0.85	7.5±0.79
RBC (10 µl)	8.0±0.43	7.7±0.55	6.9±0.62	8.7±0.52	7.4±0.75	7.4±0.58
HGB(g/dl)	14±0.55	15±0.45	15±0.65	12±0.67	14±0.78	13±0.70
HCT(%)	46±0.93	44±1.5	44±1.2	43±0.77	44±0.72	47±0.91
MCV(fL)	55±1.4	56±1.7	56±1.9	51±1.9	57±1.2	55±1.2
MCH(pg)	19±0.34	18±0.36	19±0.53	20±0.81	18±0.40	18±0.62
MCHC (g/dl)	33±0.76	33±0.97	34±0.33	31±0.96	34±0.50	33±0.69
PLT (10 ³ μl)	770±71	680±38	680±38	665±66	720±34	640±64
LYMPH (%)	65±1.3	67±1.0	68±1.4	69±1.5	68±0.98	65±1.3
MONO (%)	4.4±0.22	5.8±0.43	4.2±0.24	4.9±0.28	4.1±0.36	5.5±0.44
GR(%)	27±0.76	22±0.66	33±0.94	21±0.37	31±1.1	29±1.1
RDW(%)	13±2.7	13±1.3	16±1.7	17±1.8	16±1.7	15±1.1

PCT(%)	0.72±0.17	0.78±0.15	0.44±0.14	0.57±0.13	0.65±0.12	0.58±0.11
MPV(fL)	8.6±0.75	7.8±1.2	8.5±0.75	8.1±0.45	8.5±0.76	8.1±0.75
PDW(%)	16±1.8	16±2.1	19±2.1	17±1.2	17±1.8	16±1.7

SUMMARY AND CONCLUSION

Skin irritation study and acute/sub-acute dermal toxicity study were conducted toensure safety of prepared hemostatic gauzes. No adverse dermal response or histopathological changes were observed in animals after application of test gauzes coated with either xanthan gum or gum tragacanth. Single / repeated dose of both gums at 2000mg/kg and 1000mg/kg respectively showed no significant toxicity. The results indicate safety of the gum-coated gauzes without any adverse effects.

Test gauzes coated with either Xanthan gum or Gum tragacanth exhibited good mechanical properties; capacity to hold blood exudates for longer time; were found to be non-irritable to skin; did not induce any toxicity, and also had the ability to protect the wound against bacterial infection by virtue of having a broad-spectrum antibiotic loaded onto them. Of all the test combinations studied, gauzes coated with 2- 4% gum tragacanth were found to be the best in clotting the blood in least time as compared to other gum combinations as well as commercially available dressing Surgispon. So, the results of the study suggest the potential of gum tragacanth to be developed into a suitable hemostatic dressing material with antibacterial properties.

REFERENCES

- Abdullah, E., Taha, S., Sulaiman, N., & Ahmed, M., (2022). "Impact of acacia arabica topical gel on skin wound healing: An experimental study," *Pharmacia.*, 69(1), pp. 77-83.
- Achneck, H. E., Sileshi, B., Jamiolkowski, R. M., Albala, D. M., Shapiro, M. L., & Lawson, J. H., (2010), "A comprehensive review of topical hemostatic agents: efficacy and recommendations for use," *Annals of surgery.*, 251(2), pp. 217-228.
- Balaghi, S., Mohammadifar, M. A., & Zargaraan, A., (2010), "Physicochemical and rheological characterization of gum tragacanth exudates from six species of Iranian Astragalus," *Food Biophysics.*, 5, pp. 59-71.
- Cannella, Vincenza., Roberta, Altomare., Gabriele, Chiaramonte., Santina, Di Bella., Francesco Mira., Laura Russotto., Patrizia Pisano., and Annalisa Guercio., (2019), "Cytotoxicity evaluation of endodontic pins on L929 cell line,". *BioMed Research International*, 2019.
- Chan LW, Kim CH, Wang X, Pun SH, White NJ, Kim TH., (2016), "PolySTAT- modified chitosan gauzes for improved hemostasis in external hemorrhage," *Acta Biomater.*, 31, pp. 178–185.
- Clay JG, Grayson JK, Zierold D., (2010), "Comparative testing of new hemostatic agents in a swine model of extremity arterial and venous hemorrhage," *Mil Med* 175(4), pp. 280–284.
- Dalmoro, A., Barba, A. A., Lamberti, G., Grassi, M., & d'Amore, M., (2012), "Pharmaceutical applications of biocompatible polymer blends containing sodium alginate," *Advances in Polymer Technology.*, 31(3), pp. 219-230.
- Edwards, J. V., Graves, E., Prevost, N., Condon, B., Yager, D., Dacorta, J., & Bopp, A., (2020), "Development of a nonwoven hemostatic dressing based on unbleached cotton: a de novo design approach," *Pharmaceutics.*, 12(7), pp. 609.
- Elsabahy, M., & Hamad, M. A., (2021), "Design and preclinical evaluation of chitosan/kaolin nanocomposites with enhanced hemostatic efficiency," *Marine Drugs.*, 19(2), pp. 50.
- Gavlighi, H. A., Meyer, A. S., Zaidel, D. N., Mohammadifar, M. A., & Mikkelsen, J. D., (2013), "Stabilization of emulsions by gum tragacanth (Astragalus spp.) correlates to the galacturonic acid content and methoxylation degree of the gum," *Food Hydrocolloids.*, 31(1), pp. 5-14.

- Hajosch, R., Suckfuell, M., Oesser, S., Ahlers, M., Flechsenhar, K., & Schlosshauer, B., (2010)., "A novel gelatin sponge for accelerated hemostasis," Journal of Biomedical Materials Research Part B: Applied Biomaterials., 94(2), pp. 372-379.
- Kushwah H, Sandal N, Chauhan M, et al., (2021), "Pharmacological comparison of four biopolymeric natural gums as hemostatic agents for management of bleeding wounds: preliminary in vitro and in vivo results," Futur J Pharm Sci., **7**(1), pp. 89.
- Lankalapalli, S., & Sandhala, D., (2019), "A review on natural gums and their use as pharmaceutical excipients," International Journal of Pharmaceutical Sciences and Research., 10(12), pp. 5274-5283.
- Lawrence, JF., & Iyengar, JR., (1985), "Gas chromatographic determination of polysaccharide gums in foods after hydrolysis and derivatization," Journal of Chromatography., 350, pp. 237–244.
- Mackman, N., Tilley, R. E., & Key, N. S., (2007), "Role of the extrinsic pathway of blood coagulation in hemostasis and thrombosis," Arteriosclerosis, thrombosis, and vascular biology., 27(8), pp. 1687-1693.
- Nehra, A., Biswas, D., Siracusa, V., & Roy, S., (2023), "Natural gum-based functional bioactive films and coatings: A Review," International Journal of Molecular Sciences., 24(1), pp. 485.
- Neubauer, K., & Zieger, B, (2022), "Endothelial cells and coagulation," Cell and tissue research., 387(3), pp. 391-398.
- Nugraha SE, Suwarso E, Yuandani., (2018), "In vitro hemostatic activity of ethanol extracts of Beetroot (Beta vulgaris L.) in blood male albino rat," J Innov Pharma Biol Sci., 5(1), pp. 34-36.
- Palm, MD., Altman, JS., (2008), "Topical hemostatic agents: a review," *Dermatologic Surgery.*, 34(4), pp. 431– 445.
- Palta, S., Saroa, R., & Palta, A., (2014), "Overview of the coagulation system," *Indian journal of anaesthesia*. **58**(5), pp. 515.
- Peralta, E. (2018), "Overview of topical hemostatic agents and tissue adhesives," UpToDate. Waltham (MA): UpToDate.
- Periayah, M. H., Halim, A. S., & Saad, A. Z. M., (2017), "Mechanism action of platelets and crucial blood coagulation pathways in hemostasis," International journal of hematology-oncology and stem cell research., **11**(4), pp. 319.
- Peyvandi, F., Garagiola, I., & Baronciani, L., (2011), "Role of von Willebrand factor in the haemostasis," Blood Transfusion, 9(Suppl 2), s3.
- Pilli, V. S., (2018), "Understanding the clotting cascade, regulators, and clinical modulators of coagulation," In Hematology-Latest Research and Clinical Advances. IntechOpen.
- Recinos, G., Inaba, K., Dubose, J., Demetriades, D., & Rhee, P., (2008), "Local and systemic hemostatics in trauma: a review," Ulusal Travma ve Acil Cerrahi Dergisi., 14(3), pp. 175.
- Reduan, F. H., Shaari, R. M., Sayuti, N. S. A., Mustapha, N. M., Abu Bakar, M. Z., Sithambaram, S., & Hamzah, H., (2020), "Acute and subacute dermal toxicity of ethanolic extract of Melastoma malabathricum leaves in Sprague-Dawley rats," *Toxicological Research.*, **36**, pp. 203-210.
- Savage, B., Cattaneo, M., & Ruggeri, Z. M., (2001), "Mechanisms of platelet aggregation," Current *opinion in hematology.*, **8**(5), pp. 270-276.
- Schonauer, C., Tessitore, E., Moraci, A., Barbagallo, G., & Albanese, V., (2005), "The use of local agents: bone wax, gelatin, collagen, oxidized cellulose," Haemostasis in spine surgery., pp. 89-96.
- Scognamiglio, F., Travan, A., Rustighi, I., Tarchi, P., Palmisano, S., Marsich, E., ... & Paoletti, S., (2016)., "Adhesive and sealant interfaces for general surgery applications," Journal of Biomedical Materials Research *Part B: Applied Biomaterials*, **104**(3)., pp. 626-639.

- Soufane, S., Bouzidi, A., Mahdeb, N., & Krache, S., (2018)., "Evaluation of acute and subacute toxicity of fruit methanolic extract from Citrullus colocynthis in male albino rats"
- Spotnitz, William D., and Sandra Burks., (2008), "Hemostats, sealants, and adhesives: components of the surgical toolbox," *Transfusion.*, **48**(7), pp. 1502-1516.
- Torres, M. D., Moreira, R., Chenlo, F., & Vázquez, M. J., (2012), "Water adsorption isotherms of carboxymethyl cellulose, guar, locust bean, tragacanth and xanthan gums," *Carbohydrate polymers.*, **89**(2), pp. 592-598.
- Truffa Giachet, F., Periolatto, M., Sanchez Ramirez, D. O., Carletto, R. A., Varesano, A., Vineis, C., & Bongiovanni, R. (2019). "Stability of ultraviolet-cured chitosan
- coating on cotton gauze for water filtration," Journal of Industrial Textiles, 48(8), 1384-1396.
- Trott, A. T., (1997), "Cyanoacrylate tissue adhesives: an advance in wound care," *Jama.*, 277(19), pp. 1559-1560.
- Yang, X., Liu, W., Li, N., Wang, M., Liang, B., Ullah, I., ... & Shi, C., (2017), "Design and development of polysaccharide hemostatic materials and their hemostatic mechanism," *Biomaterials science.*, 5(12), pp. 2357-2368.
- Zhong, Y., Hu, H., Min, N., Wei, Y., Li, X., & Li, X., (2021), "Application and outlook of topical hemostatic materials: a narrative review," *Annals of Translational Medicine*.

