

Progress of Gallic Acid Derived Microcomposite Gel Systems for Effective Wound Healing: A Review

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Abstract

Management of chronic wounds continues to be a formidable clinical problem, demanding novel therapeutic strategies that target various stages of the healing cascade. Natural polyphenolic compounds such as gallic acid have been attracting interest as potential wound healing agents because of their multiple therapeutic activities. This review discusses in detail the preparation, characterization, application of gallic acid-loaded microcomposite gels, and their in vitro and in vivo studies, and focuses especially on chitosan-alginate matrix formulations. Incorporation of GA in biocompatible polymer matrices is a strategy to overcome GA's poor solubility in water and low bioavailability, in general. This review comprehensively summarizes the available understanding on formulation approaches, physicochemical characterization methods, release kinetics, and therapeutic potentials of gallic acid-based microcomposite systems. The study results indicate that ionotropic gelation approaches incorporating optimized polymer blends are able to develop stable colloidal forms with favourable particle size distribution, improved EE and controlled release patterns. The pseudoplastic rheology and the physiologically compatible pH ranges of these formulations result in enhanced patient compliance and therapy. Future directions of research therefore should involve comprehensive in vivo studies and real clinical validation of safety and efficacy that would be most welcomed for such new systems of drug delivery.

Key Words:

Gallic Acid, Microcomposite Gels, Chitosan-Alginate Matrices, Wound Healing, Controlled Drug Delivery, Ionic Gelation, Biocompatibility

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I. INTRODUCTION

Wound healing is one of the most complex biological processes cascades of cellular and molecular events by which integrity and function are restored to injured tissue. Normal healing has been arbitrarily divided into four overlapping phases: the haemostasis phase, the inflammatory phase, the proliferative phase, and the remodeling of tissue. Each step needs exact control of cell actions,

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growth factor signals, and changes in the outer matrix for best healing results ^[1]. However, in many parts of the world chronic wounds present great challenges to health care systems which in turn affect millions of patients and bear large scale economic impacts on health care infrastructure. These persistent wounds which we see put forth by patients often are a result of what we know to be underlying pathophysiological conditions such as diabetes mellitus, vascular insufficiency and immunocompromised states which in turn disrupt the normal healing processes and which in turn cause patients to have very long recovery times ^[2].

What we see is that the complex picture of chronic wound pathophysiology has in turn caused researchers to develop very innovative therapeutic strategies which in fact address many aspects of impaired healing at the same time. Also, what we have seen is that traditional wound care methods which tend to focus on a single therapeutic target may in fact be found to be inadequate for the very multi factor health issues which we see in chronic wound care. Thus, there is a growing focus on development of wide spectrum treatment approaches which may include modulation of inflammation, promotion of angiogenesis, increase in collagen synthesis, and also which are able to put up a good fight against microorganisms in the same therapeutic entity ^[3].

In the field of wound healing research natural polyphenols have seen great attention for their many health benefits and also very good safety records. These from the natural world have many therapeutic actions which in turn support the complex needs of the wound healing process. Among many polyphenols which are out there, gallic acid (3,4,5-trihydroxybenzoic acid) has come forth as a very promising player in wound care due to its noted roles as an antioxidant, anti-inflammatory, and antimicrobial ^[4].

Gallic acid is found as a naturally existing plant species in the certain plants include tea leaves, grape seeds, bark of oak as well as in different medicinal herbs. Its special chemical properties and biological functions are due to the presence of three hydroxyl groups and one carboxyl group on a benzene ring as its chemical structure. Its free radical scavenging, inflammatory pathway modulation, anti-infective activities have promising features as a candidate for topical wound healing applications ^[5].

Therapeutical value of gallic acid has been restricted by various pharmacokinetic obstacles. The substance has limited water solubility, degrades quickly under physiological conditions, and has poor bioavailability in the event of topical application. The above limitations have led to the design of novel drug delivery systems, which can protect the gallic multiple bond of gallic acid against

degradation, and facilitate externally directed penetration in the targeted tissue and more controlled release profiles [6].

Microcomposite gel systems have become novel drug delivery matrix to overcome such obstacles efficiently. These systems not only possess the advantages of microencapsulation technology and the aid of natural/synthetic hydrogel matrices, but also provide higher stability, controlled drug release, and better bioavailability. The use of gallic acid in micro composite gel system, has been realized as a strategic approach to achieve efficiency of drug against its free drug limitations [7].

Selection of suitable polymer matrices is deemed necessary for successful preparation of Gallic-acid loaded microcomposite gels. Chitosan and alginate have been widely studied as matrix materials because of their biocompatibility, biodegradability, and natural wound healing ability. Cationic mucoadhesive chitosan, obtained by deacetylation of chitin, also has antimicrobial effect. Alginate, derived from brown seaweeds, has a great ability to gel and is generally biocompatible. The combination of these polymers also has synergistic effects to maintain formulation stability and therapeutic efficacy [8].

This wide-ranging review is designed to collate the latest progress of the gallic acid-loaded microcomposite gels systems, especially involved in the fabrication, characterization and therapeutic applications of wound healing. Formulation approaches, analytical characterization methods, drug release mechanism, and therapeutic response of these novel drug delivery system are reviewed.

II. GALLIC ACID: THERAPEUTIC PROPERTIES AND WOUND HEALING MECHANISMS

i. Chemical Structure and Properties

Gallic acid (GA) is a phenolic acid compound naturally present in plants and has a molecular formula of $C_7H_6O_5$ 170.12 g/mol. Its organic structure is a benzene ring with three hydroxyl groups attached (positions 1, 2, 3) and a carboxylic acid at position 1. The special conformational structure is responsible for the multiple biological and chemical activities of the structure. Gallic acid can develop the formation of the extensive networks of hydrogen bonds because of the several hydroxyl moieties it contains, that effect its solubility properties, interaction with microorganic molecules [9].

The compound suffers from poor water solubility (approximately 1.2 g/L at 25°C) and it is difficult to develop pharmaceutical formulations of this compound. There is, however, a considerably higher solubility of the substance in organic solvents and in an alkaline environment. This is reasonable since the pKa of gallic acid (pKa = ~4.4) indicates its slightly acidic character with weak capacity to be ionized within a pH environment close to the physiological pH. These physicochemical properties warrant careful investigation during formulation development to facilitate ease of drug loading and release ^[10].

ii. Antioxidant Activity

Gallic acid-derived antioxidants are mainly ascribed to its phenolic hydroxyl groups, which have hydrogen atoms to donate to scavenge free radicals and reactive oxygen species. The molecule has higher radical scavenging ability than most synthetic antioxidants and is therefore particularly useful in wound healing, in which oxidative stress can retard the healing process ^[11]. Within the realm of wound healing, oxidative stress fails to foster the healing process, as it keeps the inflammatory response in check. For instance, excessive production of reactive oxygen species leads to reactions with proteins, lipids, and nucleic acids, which ultimately inhibit cellular functions and promote slow healing through enhanced inflammation. Thus, the antioxidant properties of gallic acid to scavenge such reactive species and restore redox balance is integral to its wound healing properties ^[12].

iii. Anti-inflammatory Properties

Gallic acid has potent anti-inflammatory effects through several molecular mechanisms. For instance, gallic acid inhibits pro-inflammatory enzyme activity by cyclooxygenase and lipoxygenase, which otherwise facilitate the production of inflammatory mediators like prostaglandins and leukotrienes. In addition, the polyphenol exerts influence over nuclear factor-kappa B (NF-κB) pathways central to signalling cascades for inflammatory gene expression ^[13].

Controlled inflammation is vital for normal wound healing. Chronic wounds occur when the inflammatory response is out of control and sustained, not allowing for proper tissue generation and restoration. Therefore, gallic acid's properties to modulate the inflammatory response but phenolic constituents that induce pro-healing factors make it an ideal component for any wound healing agent ^[14].

iv. Antimicrobial Activity

Gallic acid has antimicrobial properties against bacteria, fungi, and even viruses. The mechanism of antimicrobial action of the compound is complex-membrane disruption, peroxidase and polyphenol oxidase inhibition, and the generation of reactive oxygen species, which all contribute to damage and destruction of cellular integrity [15].

Often, wounds become infected with bacteria. Bacterial infections are a major concern and complication in wound healing, causing delayed wound repair, longer time to heal, complications, and increased risk of death. Gallic acid possesses a variety of antibacterial properties for gram-positive and gram-negative bacteria. In particular, it has an impact on *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*—the top three common bacterial microorganisms which populate wound infections. Thus, by adding gallic acid into any formulation for wound healing, it provides another level of efficacy [16].

v. Wound Healing Mechanisms

The wound healing effects gallic acid displays are partially due to its antioxidant, anti-inflammatory, and antimicrobial activities, and to its direct effects on cell processes required for tissue regeneration. The compound can activate the collagen synthesis of fibroblasts, have the function of promoting angiogenesis and inhibiting growth factor can potentiate the cellular proliferation and migration effects [17].

Their potential to enhance the synthesis of collagen is critical in wound repair because collagen is the main structural protein in healed tissue. It appears capable of increasing the expression of collagen genes and the activity of structural enzymes for collagen cross-linking to increase using the tensile strength of healed wounds [18].

III. MICROCOMPOSITE GEL SYSTEMS: DESIGN AND DEVELOPMENT STRATEGIES**i. Principles of Microcomposite Gel Technology**

Microcomposite gel systems are a novel form of drug delivery in which the advantages of both microencapsulation and hydrogel technologies are incorporated. These devices usually comprise drug-loaded microparticles, suspended in a hydrogel medium, for double-level regulation of drug

release kinetics. Microparticles are drug-responsible, whereas the hydrogel matrix serves as the secondary release and formulation modifying tool (spreading and adhesiveness) [19].

Multiple design elements must be considered when creating microcomposite gel systems because they depend on polymer selection and drug-polymer compatibility and particle size distribution and release kinetics. The combined components of these formulations produce sustained drug delivery systems which maintain stability and provide better therapeutic effects than standard gel medications [20].

ii. Chitosan-Alginate Matrix Systems

The combination of chitosan with alginate produces a drug delivery system that benefits from their complementary properties. The cationic polysaccharide chitosan originates from chitin deacetylation while alginate derives from brown seaweed as an anionic polysaccharide. The electrostatic attraction between these oppositely charged polymers leads to stable polyelectrolyte complexes which exhibit improved mechanical strength [21].

The combination of chitosan and alginate has many benefits for wound healing applications. Chitosan gives antimicrobial properties, mucoadhesive qualities, and helps stop bleeding. Alginate adds the ability to form gels, is biocompatible, and promotes healing. Together, these materials create systems that improve drug loading, control release rates, and enhance treatment outcomes [22].

iii. Ionic Gelation Technique

The ionic gelation technique is a gentle and effective way to prepare chitosan-alginate microcomposite gels. This method depends on forming ionic links between polymer chains and multivalent ions, usually calcium ions. It involves adding polymer solutions sequentially under controlled conditions, then introducing a cross-linking agent to form gel matrices [23].

The ionic gelation process has many advantages. It uses mild conditions that help maintain drug stability, allows for scaling up production, and creates particles with narrow size ranges. This technique allows precise control over particle size and encapsulation efficiency by optimizing factors like polymer concentrations, stirring speed, and cross-linking agent concentration [24].

IV. CHARACTERIZATION TECHNIQUES FOR MICROCOMPOSITE GELS

i. Spectroscopic Analysis

Spectroscopic techniques are vital for characterizing gallic acid-loaded microcomposite gels. UV-visible spectroscopy allows for quantitative analysis of drug content and release studies. The absorption peak of gallic acid at around 270 nm enables sensitive and specific measurement in various media [25].

Fourier Transform Infrared (FTIR) spectroscopy provides insights into drug-polymer interactions and the structural properties of microcomposite gels. This technique identifies chemical bonding patterns, checks drug-polymer compatibility, and confirms successful encapsulation without harmful chemical reactions. FTIR analysis is especially useful for examining hydrogen bonding between gallic acid and polymer matrices [26].

ii. Particle Size and Zeta Potential Analysis

Dynamic light scattering techniques give important information about particle size distribution and the stability of microcomposite gels. Optimal particle sizes for topical use usually range from 100 to 500 nm. This size ensures good penetration while keeping stability. A polydispersity index value below 0.3 indicates a narrow size range and a uniform formulation [27].

Zeta potential measurements evaluate the surface charge of particles, which affects their stability and potential interactions with cells. Positive zeta potential values above ± 25 mV generally signal good stability and less tendency to clump together. Chitosan-based systems often show positive zeta potentials due to protonated amino groups in acidic environments [28].

iii. Rheological Characterization

Rheological studies provide key insights into the flow behaviour and mechanical properties of microcomposite gels. Most topical formulations show non-Newtonian flow behaviour, especially pseudoplastic or shear-thinning properties. These traits make it easy to apply and spread the gels. Rheological parameters affect patient acceptance and treatment effectiveness [29].

Evaluating rheological properties involves measuring viscosity at various shear rates, determining flow indices, and examining thixotropic behaviour. These factors directly affect spreadability, adherence, and drug release rates of topical formulations [30].

V. DRUG RELEASE MECHANISMS AND KINETICS

i. Release Kinetics Models

Drug release from microcomposite gel systems generally follows complex patterns that different mathematical models can describe. Commonly used models include zero-order, first-order,

Higuchi, and Korsmeyer-Peppas. Each model helps understand the release mechanisms and optimize formulation parameters [31].

Zero-order kinetics show constant drug release rates that don't depend on drug concentration, which is ideal for sustained release. First-order kinetics indicate release that depends on concentration, while Higuchi kinetics suggest diffusion-controlled release from matrix systems. The Korsmeyer-Peppas model reveals details about the release mechanism, differentiating between Fickian diffusion, anomalous transport, and polymer relaxation-controlled release [32].

ii. Biphasic Release Patterns

Many microcomposite gel systems display biphasic release patterns with an initial burst followed by sustained release. The burst gives quick therapeutic effects while the sustained phase keeps therapeutic levels over longer periods. This pattern is particularly useful for wound healing applications, where both immediate and long-lasting effects are needed [33].

The biphasic behaviour comes from the dual structure of microcomposite systems. The drug associated with the surface causes burst release, while the drug embedded in the matrix contributes to sustained release. The balance between these phases can be adjusted through formulation optimization [34].

iii. Factors Affecting Drug Release

Several factors influence drug release from microcomposite gel systems, such as polymer concentration, cross-linking density, particle size, drug loading, and environmental conditions. Higher polymer concentrations often lead to slower release rates because of longer paths for diffusion and less mobility for the drug [35].

Cross-linking density impacts matrix porosity and drug diffusion rates, with more cross-linking generally leading to slower release. Particle size affects the surface area available for drug release, with smaller particles typically allowing for faster release. Drug loading influences the concentration gradient driving diffusion [36].

VI. THERAPEUTIC APPLICATIONS AND CLINICAL POTENTIAL

i. Wound Healing Applications

Gallic acid-loaded microcomposite gels show great potential for various wound healing applications, including acute wounds, chronic ulcers, and surgical cuts. The diverse therapeutic properties of gallic acid, combined with the controlled release features of microcomposite systems, create effective treatment options that address several aspects of wound healing [37].

The controlled release of gallic acid from these gels ensures that therapeutic levels stay maintained at wound sites while reducing systemic exposure and potential side effects. This method of localized drug delivery enhances treatment effectiveness while improving patient safety.

ii. Advantages Over Conventional Formulations

Microcomposite gel systems provide several benefits compared to traditional topical formulations. They have better drug stability, controlled release profiles, improved bioavailability, and less frequent application needs. These advantages lead to greater patient compliance and better treatment results. The protective nature of polymer matrices keeps encapsulated gallic acid safe from breakdown, helping the drug retain its potency over time. Controlled release reduces the need for frequent applications, which improves patient convenience and compliance.

VII. FUTURE PERSPECTIVES AND RESEARCH DIRECTIONS

i. Clinical Translation Requirements

Moving gallic acid-loaded microcomposite gels from the lab to clinical use requires thorough safety and effectiveness evaluations through well-designed preclinical and clinical trials. These studies should examine biocompatibility, potential skin irritation, treatment efficacy, and long-term safety.

Regulatory requirements for topical drug products include stability tests, quality control protocols, and standard manufacturing practices. Meeting these standards needs robust analytical methods and consistent production processes to guarantee product safety and reliability.

ii. Emerging Technologies

Emerging technologies like nanotechnology, smart materials, and personalized medicine offer potential for further improving gallic acid-loaded microcomposite gels. These innovations may enable responsive drug release, targeted delivery, and customized treatment strategies.

Incorporating biomarker-responsive elements, stimuli-sensitive polymers, and advanced characterization techniques could lead to better wound healing formulas with enhanced treatment capabilities and improved patient outcomes.

VIII. CONCLUSION

Gallic acid-loaded microcomposite gel systems are a promising advancement in topical drug delivery for wound healing. They effectively combine the therapeutic properties of gallic acid with the controlled release features of chitosan-alginate matrices. This combination overcomes the inherent limitations of the compound and boosts its therapeutic potential. Comprehensive characterization shows favourable properties, controlled drug release, and clinical application potential.

Developing these innovative drug delivery systems provides valuable insights into pharmaceutical nanotechnology and offers promising solutions to advance wound care. However, further research through in vivo studies and clinical trials is crucial for validating the efficacy and safety of these formulations. The future success of gallic acid-loaded microcomposite gels relies on ongoing research, compliance with regulations, and effective clinical translation.

IX. REFERENCES

1. Gurtner, G. C., Werner, S., Barrandon, Y., & Longaker, M. T. (2008). Wound repair and regeneration. *Nature*, 453(7193), 314-321.
2. Sen, C. K., Gordillo, G. M., Roy, S., Kirsner, R., Lambert, L., Hunt, T. K., & Longaker, M. T. (2009). Human skin wounds: a major and snowballing threat to public health and the economy. *Wound repair and regeneration*, 17(6), 763-771.
3. Mssillou, I., Bakour, M., Slighoua, M., Laaroussi, H., Saghrouchni, H., Amrati, F. E. Z., & Derwich, E. (2022). Investigation on wound healing effect of Mediterranean medicinal plants and some related phenolic compounds: A review. *Journal of ethnopharmacology*, 298, 115663.
4. Yang, D. J., Moh, S. H., Son, D. H., You, S., Kinyua, A. W., Ko, C. M., & Kim, K. W. (2016). Gallic acid promotes wound healing in normal and hyperglucidic conditions. *Molecules*, 21(7), 899.
5. Chanwitheesuk, A., Teerawutgulrag, A., Kilburn, J. D., & Rakariyatham, N. (2007). Antimicrobial gallic acid from *Caesalpinia mimosoides* Lamk. *Food chemistry*, 100(3), 1044-1048.
6. da Rosa, C. G., Borges, C. D., Zambiasi, R. C., Nunes, M. R., Benvenutti, E. V., da Luz, S. R., & Rutz, J. K. (2013). Microencapsulation of gallic acid in chitosan, β -cyclodextrin and xanthan. *Industrial crops and products*, 46, 138-146.

7. Naeem, A., Yu, C., Zhu, W., Chen, X., Wu, X., Chen, L., ... & Guan, Y. (2022). Gallic acid-loaded sodium alginate-based (polyvinyl alcohol-co-acrylic acid) hydrogel membranes for cutaneous wound healing: synthesis and characterization. *Molecules*, 27(23), 8397.
8. Abasalizadeh, F., Moghaddam, S. V., Alizadeh, E., Akbari, E., Kashani, E., Fazljou, S. M. B., & Akbarzadeh, A. (2020). Alginate-based hydrogels as drug delivery vehicles in cancer treatment and their applications in wound dressing and 3D bioprinting. *Journal of biological engineering*, 14(1), 8.
9. Badhani, B., Sharma, N., & Kakkar, R. (2015). Gallic acid: A versatile antioxidant with promising therapeutic and industrial applications. *Rsc Advances*, 5(35), 27540-27557.
10. Daglia, M. (2012). Polyphenols as antimicrobial agents. *Current opinion in biotechnology*, 23(2), 174-181.
11. Hussain, T., Tan, B., Yin, Y., Blachier, F., Tossou, M. C., & Rahu, N. (2016). Oxidative stress and inflammation: what polyphenols can do for us. *Oxidative medicine and cellular longevity*, 2016(1), 7432797.
12. Marcelino, P., Marinho, H. S., Campos, M. C., Neves, A. R., Real, C., Fontes, F. S., & Corvo, M. L. (2017). Therapeutic activity of superoxide dismutase-containing enzymosomes on rat liver ischaemia-reperfusion injury followed by magnetic resonance microscopy. *European Journal of Pharmaceutical Sciences*, 109, 464-471.
13. Kroes, B. V., Van den Berg, A. J. J., Van Ufford, H. Q., Van Dijk, H., & Labadie, R. P. (1992). Anti-inflammatory activity of gallic acid. *Planta medica*, 58(06), 499-504.
14. Kotsantis, P., Papadimitropoulos, A., Drakopoulos, A., Vlachojannis, J. G., & Katsoris, P. (2013). Albumin upregulates eNOS mRNA through ETRA/B in human proximal tubular epithelial cells. *J Nephrol*, 26(3), 510-6.
15. Borges, A., Ferreira, C., Saavedra, M. J., & Simões, M. (2013). Antibacterial activity and mode of action of ferulic and gallic acids against pathogenic bacteria. *Microbial drug resistance*, 19(4), 256-265.
16. Nayaka, H. B., Londonkar, R. L., Umesh, M. K., & Tukappa, A. (2014). Antibacterial attributes of apigenin, isolated from *Portulaca oleracea* L. *International journal of bacteriology*, 2014(1), 175851.
17. Kim, S. H., Jun, C. D., Suk, K., Choi, B. J., Lim, H., Park, S., & Shin, T. Y. (2006). Gallic acid inhibits histamine release and pro-inflammatory cytokine production in mast cells. *Toxicological Sciences*, 91(1), 123-131.

18. Kasozi, D. M., Gromer, S., Adler, H., Zoicher, K., Rahlfs, S., Wittlin, S., & Becker, K. (2011). The bacterial redox signaller pyocyanin as an antiplasmodial agent: comparisons with its thioanalog methylene blue. *Redox Report*, *16*(4), 154-165.
19. Bashir, S., Hina, M., Iqbal, J., Rajpar, A. H., Mujtaba, M. A., Alghamdi, N. A., & Ramesh, S. (2020). Fundamental concepts of hydrogels: Synthesis, properties, and their applications. *Polymers*, *12*(11), 2702.
20. Wu, J., Zheng, Y., Song, W., Luan, J., Wen, X., Wu, Z., & Guo, S. (2014). In situ synthesis of silver-nanoparticles/bacterial cellulose composites for slow-released antimicrobial wound dressing. *Carbohydrate polymers*, *102*, 762-771.
21. Jayakumar, R., Prabakaran, M., Kumar, P. S., Nair, S. V., & Tamura, H. J. B. A. (2011). Biomaterials based on chitin and chitosan in wound dressing applications. *Biotechnology advances*, *29*(3), 322-337.
22. Saberian, M., Roudsari, R. S., Haghshenas, N., Rousta, A., & Alizadeh, S. (2024). How the combination of alginate and chitosan can fabricate a hydrogel with favorable properties for wound healing. *Heliyon*, *10*(11).
23. Omer, A. M., Ahmed, M. S., El-Subruiti, G. M., Khalifa, R. E., & Eltaweil, A. S. (2021). pH-sensitive alginate/carboxymethyl chitosan/aminated chitosan microcapsules for efficient encapsulation and delivery of diclofenac sodium. *Pharmaceutics*, *13*(3), 338.
24. Patil, P., & Killedar, S. (2021). Chitosan and glyceryl monooleate nanostructures containing gallic acid isolated from amla fruit: targeted delivery system. *Heliyon*, *7*(3).
25. Rawat, B., & Garg, A. P. (2021). Characterization of phytochemicals isolated from Cucurbita pepo seeds using UV-VIS and FTIR spectroscopy. *Plant Archives (09725210)*, *21*(1).
26. Singh, P., Saxena, S., Singh, S. K., Chandra, S., Chandra, A., & Vijay, P. (2021). A study on association of diabetes mellitus and hypertension with their demographics and blood parameters-a pilot study. *Int J Appl Biol Pharm*, *12*, 397-408.
27. Danaei, M. R. M. M., Dehghankhold, M., Ataei, S., Hasanzadeh Davarani, F., Javanmard, R., Dokhani, A., & Mozafari, Y. M. (2018). Impact of particle size and polydispersity index on the clinical applications of lipidic nanocarrier systems. *Pharmaceutics*, *10*(2), 57.
28. Mourya, V. K., & Inamdar, N. N. (2008). Chitosan-modifications and applications: Opportunities galore. *Reactive and Functional polymers*, *68*(6), 1013-1051.
29. Monteiro e Silva, S. A., Calixto, G. M. F., Cajado, J., De Carvalho, P. C. A., Rodero, C. F., Chorilli, M., & Leonardi, G. R. (2017). Gallic acid-loaded gel formulation combats skin

- oxidative stress: Development, characterization and ex vivo biological assays. *Polymers*, 9(9), 391.
30. Khan, M. U. A., Razaq, S. I. A., Mehboob, H., Rehman, S., Al-Arjan, W. S., & Amin, R. (2021). Antibacterial and hemocompatible pH-responsive hydrogel for skin wound healing application: In vitro drug release. *Polymers*, 13(21), 3703.
31. Peppas NA, Narasimhan B. Mathematical models in drug delivery: How modeling has shaped the way we design new drug delivery systems. *Journal of Controlled Release*. 2014; 190:75-81
32. Costa, P., & Lobo, J. M. S. (2001). Modeling and comparison of dissolution profiles. *European journal of pharmaceutical sciences*, 13(2), 123-133.
33. Wang, C., Wang, F., Liu, J., Yi, W., Zhao, Q., & Liu, Y. (2024). Transdermal drug-delivery motion-sensing hydrogels for movement recovery caused by external injury. *Chemical Engineering Journal*, 488, 150998.
34. Sallustio, V., Chiochio, I., Mandrone, M., Cirrincione, M., Protti, M., Farruggia, G., & Cerchiara, T. (2022). Extraction, encapsulation into lipid vesicular systems, and biological activity of *Rosa canina* L. bioactive compounds for dermocosmetic use. *Molecules*, 27(9), 3025.
35. Rizwan, M., Yahya, R., Hassan, A., Yar, M., Azzahari, A. D., Selvanathan, V., & Abouloula, C. N. (2017). pH sensitive hydrogels in drug delivery: Brief history, properties, swelling, and release mechanism, material selection and applications. *Polymers*, 9(4), 137.
36. Mohanty, A. K., Vivekanandhan, S., Pin, J. M., & Misra, M. (2018). Composites from renewable and sustainable resources: Challenges and innovations. *Science*, 362(6414), 536-542.
37. Lv, X., Liu, Y., Song, S., Tong, C., Shi, X., Zhao, Y., & Hou, M. (2019). Influence of chitosan oligosaccharide on the gelling and wound healing properties of injectable hydrogels based on carboxymethyl chitosan/alginate polyelectrolyte complexes. *Carbohydrate Polymers*, 205, 312-321.