Advances in Polymer-Based Controlled Release Systems for Ursolic Acid: Enhancing Bioavailability and Therapeutic Efficacy

Sonam R Thombare[1], Dr. Pankaj M. Pimpalshende[2]
[1,2]*Hi-Tech College of Pharmacy, Chandrapur, Maharashtra, 442902*

***Abstract*—Ursolic acid (UA), a naturally occurring pentacyclic triterpenoid widely found in medicinal plants, has gained significant attention due to its diverse pharmacological activities, including anti-inflammatory, anticancer, antidiabetic, and antimicrobial effects. Despite its promising therapeutic potential, the clinical application of UA is significantly limited by its poor aqueous solubility, low permeability, and consequently reduced oral bioavailability. These biopharmaceutical challenges necessitate the development of advanced drug delivery strategies to enhance its efficacy.**

Polymer-based controlled release systems have emerged as a promising approach to overcome these limitations. Various natural, semi-synthetic, and synthetic polymers such as chitosan, alginate, hydroxypropyl methylcellulose (HPMC), and Eudragit have been extensively investigated for their ability to modulate drug release, improve solubility, and enhance the stability of UA. These systems, including matrix tablets, nanoparticles, hydrogels, and lipid-polymer hybrid carriers, enable sustained drug release, maintain therapeutic plasma concentrations, and improve patient compliance. Recent advancements in polymer science, including the development of smart and stimuli-responsive polymers, have further improved the efficiency of UA delivery systems. This review comprehensively discusses the formulation strategies, mechanisms of controlled release, and evaluation parameters of polymer-based UA delivery systems. Additionally, it highlights recent research trends and technological innovations aimed at enhancing bioavailability and therapeutic outcomes.

In conclusion, polymer-based controlled release systems represent a promising platform for improving the clinical potential of ursolic acid, with future research focusing on advanced nanocarriers, large-scale production, and clinical translation.

***Index Terms*—Ursolic acid, controlled release, polymers, bioavailability, sustained release, drug delivery**

I. INTRODUCTION

Herbal and phytopharmaceutical compounds have received a lot of attention due to their wide range of therapeutic benefits and natural origin; however, their clinical use is frequently hampered by issues like poor aqueous solubility, low permeability, rapid metabolism, and variable bioavailability.[1] These restrictions have a substantial impact on their therapeutic effectiveness when given in traditional dosage forms.[2] By preserving constant medication levels in the systemic circulation, lowering dose frequency, and enhancing patient compliance, controlled release drug delivery systems have become a successful tactic to get around these problems.[3] A pentacyclic triterpenoid found in many medicinal plants, ursolic acid (UA) has several pharmacological properties, such as anti-inflammatory, anticancer, antidiabetic, and antibacterial actions.[4] UA's poor solubility and limited oral bioavailability when prepared using conventional methods impede its therapeutic utilization, despite its intriguing potential.[5] As a result, there is an increasing demand for sophisticated formulation techniques, especially polymer-based controlled release systems that can improve solubility, shield the medication from deterioration, and offer prolonged drug release.[6] With an emphasis on formulation techniques, controlled release mechanisms, and methods to enhance ursolic acid's bioavailability and therapeutic efficacy, the current study attempts to thoroughly address recent developments in polymer-based delivery systems for the drug.[7]

II. URSOLIC ACID: A PHARMACOLOGICAL OVERVIEW

Apple peels, basil, rosemary, and Ocimum sanctum are just a few of the medicinal plants and herbs that contain ursolic acid (UA), a naturally occurring pentacyclic triterpenoid.[8] Its poor water solubility is partly due to its hydrophobic structure, which makes it a member of the class of triterpenoids.[9] UA is a viable candidate for therapeutic uses because of its wide range of pharmacological properties, which include anti-inflammatory, anticancer, antidiabetic, and antibacterial effects.[10] However, a number of biopharmaceutical issues, including poor water solubility, low intestinal permeability, and substantial first-pass metabolism, which together result in low oral bioavailability, limit its therapeutic relevance.[11] These drawbacks underscore the necessity of sophisticated drug delivery strategies, especially polymer-based controlled release systems, to improve the medication's solubility, stability, and overall therapeutic efficacy.[12]

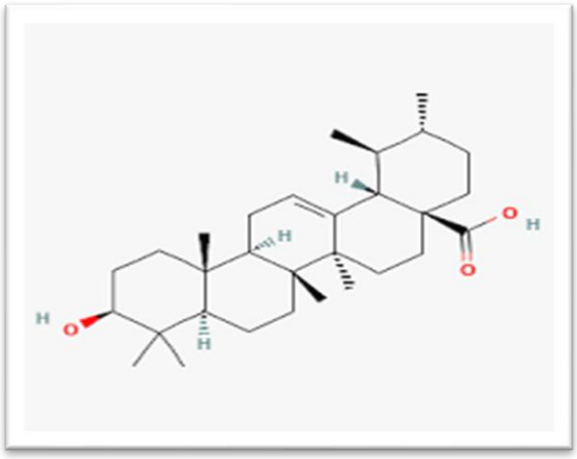

Fig.1: Structure of Ursolic acid [13]

III. CONTROLLED RELEASE DRUG DELIVERY SYSTEMS

In order to get the best possible clinical results, controlled release drug delivery systems are made to distribute therapeutic substances at a predefined rate, duration, and location.[13] These systems work on the basis of basic mechanisms like diffusion, in which the drug gradually moves through a polymer matrix; erosion, in which the polymer gradually deteriorates; and swelling, in which the polymer expands when it comes into contact with biological fluids, allowing for controlled drug release.[14] For substances like ursolic acid, which need prolonged exposure to retain therapeutic potency, these methods are especially beneficial.[15]

Reduced dose frequency, increased patient compliance, and the maintenance of steady plasma drug concentrations—all of which lessen side effects and improve treatment efficacy—are just a few benefits of controlled release systems.[16] Osmotic systems, which use osmotic pressure to control drug release, reservoir systems, which have a core drug encased in a polymeric membrane, and matrix systems, where the drug is evenly distributed within the polymer, are some of the different kinds of controlled release systems that have been developed.[17] These systems are very important for increasing the bioavailability of poorly soluble medications like ursolic acid and are essential for overcoming the drawbacks of traditional dosing forms.[18]

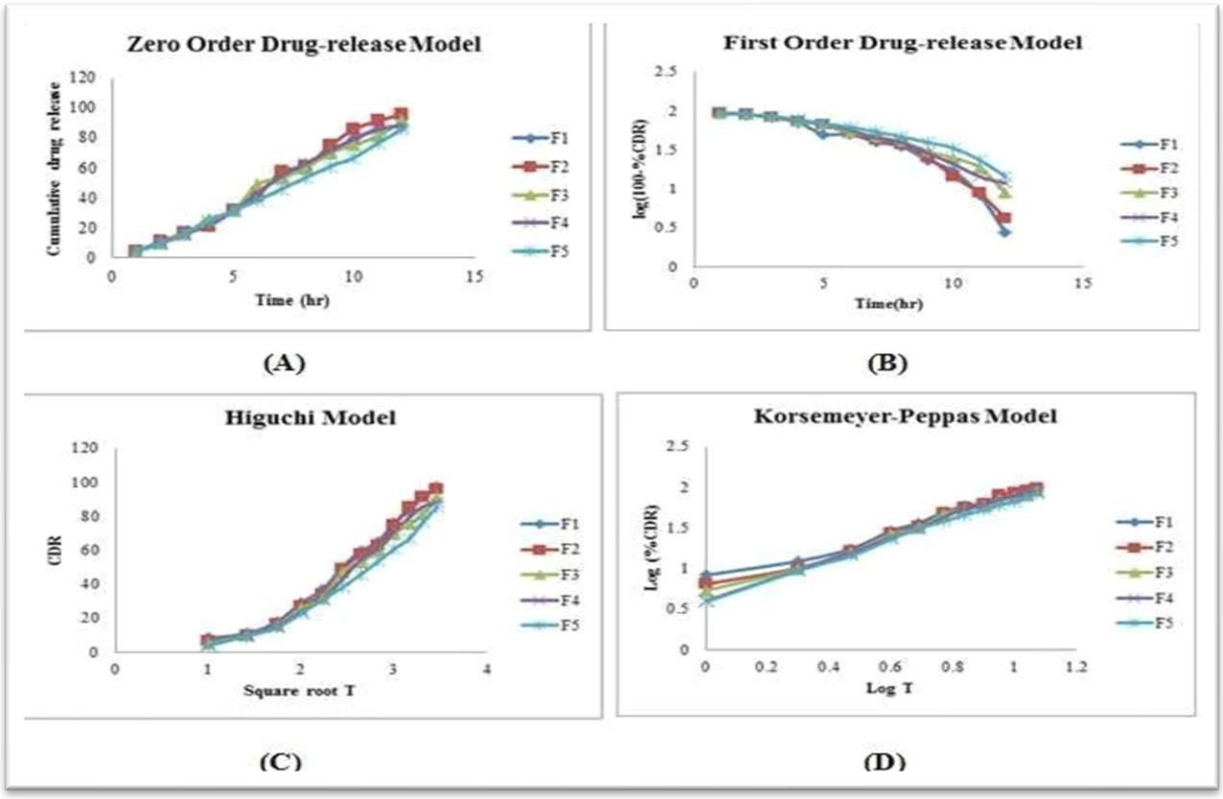

Fig.2: Drug-release kinetic studies (A) Zero order drug release kinetics, (B) First order drug release kinetics, (C) Higuchi model drug release kinetics, (D)Korsemyer peppas model drug release kinetics. [19]

IV. ROLE OF POLYMERS IN CONTROLLED RELEASE

By controlling the rate and pattern of medication release, polymers improve therapeutic efficacy and play a critical role in controlled release drug delivery systems.[20] They can be broadly divided into three categories: semi-synthetic polymers, which offer unique physicochemical features appropriate for formulation design, synthetic polymers, such as hydroxypropyl methylcellulose (HPMC) and Eudragit, and natural polymers, such as chitosan and alginate.[21] Diffusion-controlled release, in which the drug moves through the polymer matrix; swelling-controlled release, in which the polymer expands upon hydration; and erosion-controlled release, in which the polymer gradually deteriorates, are some of the mechanisms that cause drug release from polymeric systems.[22]

The choice of a suitable polymer is crucial and is influenced by variables like stability, biocompatibility, and the type of drug–polymer interactions, all of which have an impact on the formulation's overall performance and release profile.[23] Polymer-based systems are especially crucial for improving ursolic acid's solubility, preventing its degradation, and achieving regulated and prolonged drug release.[24]

V. POLYMER-BASED DELIVERY SYSTEMS FOR URSOLIC ACID

By increasing ursolic acid's solubility, stability, and bioavailability, polymer-based delivery methods have demonstrated a great deal of promise in boosting the drug's therapeutic efficacy. [25] Among these, matrix tablets—which offer benefits like ease of formulation and prolonged drug release—are frequently used.[26] Ursolic acid is evenly distributed within a polymer matrix utilizing methods including direct compression and wet granulation.[27] Furthermore, systems based on nanoparticles, such as polymeric nanoparticles and nanomicelles, offer better drug solubilization, increased cellular absorption, and tailored delivery.[28]

Another interesting strategy is the use of hydrogels, which act as regulated swelling systems that control drug release by hydrating and expanding the polymer network.[29] Moreover, lipid–polymer hybrid systems combine the advantages of polymer matrix and lipid carriers, resulting in longer release profiles, better drug encapsulation, and increased permeability.[30] All of these cutting-edge polymer-based solutions work together to overcome ursolic acid's intrinsic drawbacks and greatly increase its therapeutic efficacy.[31]

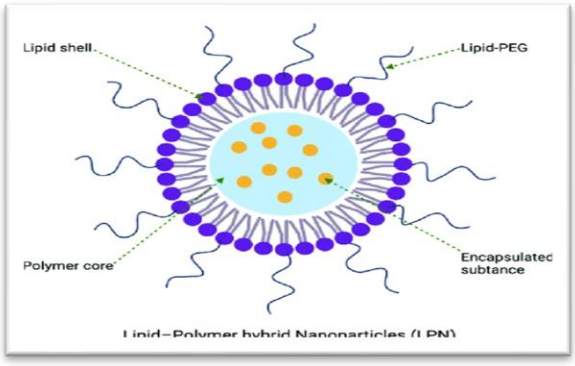

Fig.3: Lipid-polymer hybrid nanoparticles.[32]

VI. EVALUATION PARAMETERS

To guarantee quality, efficacy, and performance, extensive pre formulation, post-formulation, and stability investigations are required for the evaluation of polymer-based controlled release systems for ursolic acid. Using analytical methods like Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC), which aid in identifying potential drug–polymer interactions, preformulation studies mainly evaluate the solubility properties of ursolic acid and its compatibility with particular polymers.[33]

In order to guarantee the mechanical strength of tablets, post-formulation evaluation involves measuring physical characteristics like hardness and friability as well as the consistency of medication content for precise dosage.[34] To ascertain the dissolution profile and comprehend the release behavior of the formulation, in-vitro drug release studies are essential. The mechanism of drug release is then further examined utilizing kinetic models like zero-order, first-order, Higuchi, and Korsmeyer-Peppas.[35] Furthermore, stability tests carried out in different environmental settings assess the formulation's long-term chemical and physical stability.[36] In order to optimize polymer-based delivery systems and provide a steady, regulated release of ursolic acid with improved bioavailability and therapeutic efficacy, certain evaluation parameters are crucial.[37]

VII. BIOAVAILABILITY ENHANCEMENT APPROACHES

Given ursolic acid's poor aqueous solubility and limited absorption, increasing its bioavailability is a crucial goal in the development of efficient drug delivery methods.[38] To overcome these obstacles, a number of strategies have been investigated; among these, polymer modification is crucial for enhancing drug solubility, stability, and controlled release behavior. Better absorption is made possible by the addition of surfactants, which also help to improve wettability and dissolution rate.[39]

Ursolic acid is disseminated into a hydrophilic polymer matrix using solid dispersion techniques, which are also frequently used to enhance the solubility and dissolution characteristics of the compound.[40] Furthermore, nanoparticles, nanoemulsions, and nanomicelles are examples of nano-based delivery methods that greatly increase surface area, facilitate effective drug transport, and improve permeability across biological membranes.[41] These tactics, either separately or in combination, help ursolic acid overcome its biopharmaceutical constraints and are essential for improving its overall bioavailability and therapeutic efficacy.[42]

VIII. THERAPEUTIC APPLICATIONS OF UA CONTROLLED RELEASE SYSTEMS

Given ursolic acid's poor aqueous solubility and limited absorption, increasing its bioavailability is a crucial goal in the development of efficient drug delivery methods.[43] To overcome these obstacles, a number of strategies have been investigated; among these, polymer modification is crucial for enhancing drug solubility, stability, and controlled release behavior. Better absorption is made possible by the addition of surfactants, which also help to improve

wettability and dissolution rate.[44] Ursolic acid is disseminated into a hydrophilic polymer matrix using solid dispersion techniques, which are also frequently used to enhance the solubility and dissolution characteristics of the compound.[45]

Furthermore, nanoparticles, nanoemulsions, and nanomicelles are examples of nano-based delivery methods that greatly increase surface area, facilitate effective drug transport, and improve permeability across biological membranes.[46] These tactics, either separately or in combination, help ursolic acid overcome its biopharmaceutical constraints and are essential for improving its overall bioavailability and therapeutic efficacy.[47]

IX. CHALLENGES AND LIMITATIONS

Polymer-based controlled release methods for ursolic acid have made great strides, but a number of obstacles and restrictions prevent their broad use and commercialization.[48] The scale-up of laboratory-developed formulations to industrial manufacturing is one of the main issues because it can be challenging to maintain consistency in drug release patterns and product quality.[49] The intricacy of polymer-based systems and the requirement for substantial safety, efficacy, and quality data to satisfy approval standards make regulatory concerns another major obstacle.[50] As ursolic acid formulations may be vulnerable to physical and chemical deterioration over time, particularly under changing environmental circumstances, stability issues continue to be a significant difficulty.[51]

X. FUTURE PERSPECTIVES

With new developments aimed at improving therapeutic precision and practical application, the future of polymer-based controlled release systems for ursolic acid is bright.[52] It is anticipated that the use of personalized medicine techniques will allow for customized medication delivery systems depending on the requirements of each patient, enhancing treatment results and reducing adverse effects.[53] The bioavailability and site-specific effect of ursolic acid can be further improved by the creation of sophisticated nanocarriers, such as stimuli-responsive and targeted delivery systems, made possible by advances in nanotechnology.[54]

Moreover, efforts toward clinical translation are gaining momentum, with increasing emphasis on bridging the gap between laboratory research and large-scale production, supported by rigorous clinical studies and regulatory advancements.[55] Through creative polymer-based delivery methods, these future paths have enormous potential to make ursolic acid a more potent and extensively utilized medicinal drug.[56]

XI. CONCLUSION

In conclusion, because of its wide range of pharmacological activity, ursolic acid has considerable therapeutic potential; nevertheless, its low bioavailability and poor solubility limit its clinical utility.[57] This review emphasizes that by enhancing drug solubility, stability, and sustained release patterns, polymer-based controlled release systems provide an efficient way to get around these problems.[58] Ursolic acid's bioavailability and therapeutic efficacy have been shown to be improved by a number of strategies, including matrix systems, hydrogels, nanoparticles, and hybrid formulations.[59]

Using the right polymers is essential for controlling drug release and guaranteeing the formulation's constant performance.[60] All things considered, polymer-based delivery methods are a significant development in phytopharmaceutical research, and they have a great chance of successfully translating ursolic acid into useful therapeutic formulations with further development and clinical validation.[61]

REFERENCES

[1] Egbuna C, Mishra AP, Goyal MR, editors. Preparation of phytopharmaceuticals for the management of disorders: the development of nutraceuticals and traditional medicine. Academic Press; 2020 Nov 3.

[2] Paulsson M, Hamre Svendsen R, Andersen JK, Kälvemark Sporrong S, Andersson Y, Tho I. Challenges and Considerations in Manipulating Oral Dosage Forms in Paediatric Healthcare Settings: A Narrative Review. Acta Paediatrica. 2025 Oct;114(10):2480-9.

[3] Adepu S, Ramakrishna S. Controlled drug delivery systems: current status and future

directions. Molecules. 2021 Sep 29;26(19):5905.

[4] Sandhu SS, Rouz SK, Kumar S, Swamy N, Deshmukh L, Hussain A, Haque S, Tuli HS. Ursolic acid: a pentacyclic triterpenoid that exhibits anticancer therapeutic potential by modulating multiple oncogenic targets. Biotechnology and Genetic Engineering Reviews. 2023 Jul 3;39(2):729-59.

[5] Bakry SM, El-Shiekh RA, Hatem S, Mandour AA, El-Dessouki AM, Bishr A, Elosaily H, Mohamed AF, Elhusseiny SM. Therapeutic applications of ursolic acid: a comprehensive review and utilization of predictive tools. Future Journal of Pharmaceutical Sciences. 2025 Apr 22;11(1):48.

[6] Adepu S, Ramakrishna S. Controlled drug delivery systems: current status and future directions. Molecules. 2021 Sep 29;26(19):5905.

[7] Harwansh RK, Deshmukh R, Shukla VP, Khunt D, Prajapati BG, Rashid S, Ali N, Elossaily GM, Suryawanshi VK, Kumar A. Recent advancements in gallic acid-based drug delivery: applications, clinical trials, and future directions. Pharmaceutics. 2024 Sep 13;16(9):1202.

[8] Arulnangai R, Thabassoom HA, Banu HV, Thirugnanasambandham K, Ganesamoorthy R. Recent developments on ursolic acid and its potential biological applications. Toxicology Reports. 2025 Jun 1;14:101900.

[9] Grudzińska M, Stachnik B, Galanty A, Sołtys A, Podolak I. Progress in antimelanoma research of natural triterpenoids and their derivatives: mechanisms of action, bioavailability enhancement and structure modifications. Molecules. 2023 Nov 24;28(23):7763.

[10] Bourais I, Elmarrkechy S, Taha D, Mourabit Y, Bouyahya A, El Yadini M, Machich O, El Hajjaji S, El Boury H, Dakka N, Iba N. A review on medicinal uses, nutritional value, and antimicrobial, antioxidant, anti-inflammatory, antidiabetic, and anticancer potential related to bioactive compounds of J. regia. Food Reviews International. 2023 Oct 3;39(9):6199-249.

[11] Bhandare A, Nannor KM. Bioavailability in drug design and development: A comprehensive review. World Journal of Pharmaceutical Research. 2024 Jul 5;13(17):145-68.

[12] Eltaib L. Polymeric nanoparticles in targeted drug delivery: unveiling the impact of polymer characterization and fabrication. Polymers. 2025 Mar 21;17(7):833.

[13] Bakry SM, El-Shiekh RA, Hatem S, Mandour AA, El-Dessouki AM, Bishr A, Elosaily H, Mohamed AF, Elhusseiny SM. Therapeutic applications of ursolic acid: a comprehensive review and utilization of predictive tools. Future Journal of Pharmaceutical Sciences. 2025 Apr 22;11(1):48.

[14] Adepu S, Ramakrishna S. Controlled drug delivery systems: current status and future directions. Molecules. 2021 Sep 29;26(19):5905.

[15] Visan AI, Popescu-Pelin G, Socol G. Degradation behavior of polymers used as coating materials for drug delivery—A basic review. Polymers. 2021 Apr 14;13(8):1272.

[16] Nguyen HN, Ullevig SL, Short JD, Wang L, Ahn YJ, Asmis R. Ursolic acid and related analogues: triterpenoids with broad health benefits. Antioxidants. 2021 Jul 21;10(8):1161.

[17] Adepu S, Ramakrishna S. Controlled drug delivery systems: current status and future directions. Molecules. 2021 Sep 29;26(19):5905.

[18] Patel J, Parikh S, Patel S. Comprehensive review on osmotic drug delivery system. World J. Pharm. Res. 2021 Mar 1;10(5):523-.

[19] Wang L, Yin Q, Liu C, Tang Y, Sun C, Zhuang J. Nanoformulations of ursolic acid: a modern natural anticancer molecule. Frontiers in Pharmacology. 2021 Jul 5;12:706121.

[20] Askarizadeh M, Esfandiari N, Honarvar B, Sajadian SA, Azdarpour A. Kinetic modeling to explain the release of medicine from drug delivery systems. ChemBioEng Reviews. 2023 Dec;10(6):1006-49.

[21] Udaipuria N, Bhattacharya S. Novel carbohydrate polymer-based systems for precise drug delivery in colon cancer: Improving treatment effectiveness with intelligent biodegradable materials. Biopolymers. 2025 Jan;116(1):e23632.

[22] Saini L, Dubey A, Pal R, Pandey P, Mandal RK. Synthetic and Natural Polymers Enhancing Drug Delivery and Their Treatment: A Comprehensive Review. Journal of Drug Delivery & Therapeutics. 2024 Oct 1;14(10).

[23] Anusha A, Ponnekanti K, Tiwari R, Swapna L, Hussain MM, Siddhardha A. A review of

medicines with sustained release. World J Biol Pharmacy Health Sci. 2023; 13:221-33.

[24] Eltaib L. Polymeric nanoparticles in targeted drug delivery: unveiling the impact of polymer characterization and fabrication. Polymers. 2025 Mar 21;17(7):833.

[25] Yu X, Lu Y, Chen J, Deng Y, Liu H. Unlocking ginsenosides' therapeutic power with polymer-based delivery systems: current applications and future perspectives. Frontiers in pharmacology. 2025 Jul 10; 16:1629803.

[26] Li C, Luo Z, Feng H, Li Z. Polymers facilitating therapeutic efficacy and applications for traditional Chinese medicine. Journal of Polymer Science. 2025 Feb 15;63(4):839-63.

[27] Shah N, Oza C, Trivedi S, Shah N, Shah S. Review on sustained release matrix tablets: An approach to prolong the release of drug. JPBSR. 2015;5(3):315-21.

[28] Byeon JC, Ahn JB, Jang WS, Lee SE, Choi JS, Park JS. Recent formulation approaches to oral delivery of herbal medicines. Journal of pharmaceutical investigation. 2019 Jan 15;49(1):17-26.

[29] Begines B, Ortiz T, Pérez-Aranda M, Martínez G, Merinero M, Argüelles-Arias F, Alcudia A. Polymeric nanoparticles for drug delivery: Recent developments and future prospects. Nanomaterials. 2020 Jul 19;10(7):1403.

[30] Thang NH, Chien TB, Cuong DX. Polymer-based hydrogels applied in drug delivery: an overview. Gels. 2023 Jun 27;9(7):523.

[31] Sivadasan D, Sultan MH, Madkhali O, Almoshari Y, Thangavel N. Polymeric lipid hybrid nanoparticles (plns) as emerging drug delivery platform—A comprehensive review of their properties, preparation methods, and therapeutic applications. Pharmaceutics. 2021 Aug 18;13(8):1291.

[32] Alharbi HM. Exploring the frontier of biopolymer-assisted drug delivery: advancements, clinical applications, and future perspectives in cancer nanomedicine. Drug Design, Development and Therapy. 2024 Dec 31:2063-87.

[33] Gajbhiye KR, Salve R, Narwade M, Sheikh A, Kesharwani P, Gajbhiye V. Lipid polymer hybrid nanoparticles: a custom-tailored next-generation approach for cancer therapeutics. Molecular Cancer. 2023 Oct 3;22(1):160.

[34] Altunayar-Unsalan C. DSC and FTIR study on the interaction between pentacyclic triterpenoid lupeol and DPPC membrane. Journal of Bioenergetics and Biomembranes. 2024 Oct;56(5):553-61.

[35] Mustafa MA, Rasheed N, Islam M, Irshad I, Batool S, Naveed M, Bibi G, Nazeer J, Wajid F, Atif A, Syeda DE. Advancements in novel drug delivery systems: Techniques for pre and post formulation analysis. Journal of Pharmaceutical Research International. 2024 Aug 6;36(8):142-53.

[36] Alfei S, Schito AM, Zuccari G. Considerable improvement of ursolic acid water solubility by its encapsulation in dendrimer nanoparticles: Design, synthesis and physicochemical characterization. Nanomaterials. 2021 Aug 26;11(9):2196.

[37] González-González O, Ramirez IO, Ramirez BI, O'Connell P, Ballesteros MP, Torrado JJ, Serrano DR. Drug stability: ICH versus accelerated predictive stability studies. Pharmaceutics. 2022 Oct 28;14(11):2324.

[38] Feng T, Paul B, Chen W. Synergistic effects of co-delivery bioactive compounds using polymeric-based nanoparticles for biological activities: Recent trends. Food Quality and Safety. 2025 Oct 28: fyaf061.

[39] Khalbas AH, Albayati TM, Ali NS, Salih IK. Drug loading methods and kinetic release models using of mesoporous silica nanoparticles as a drug delivery system: A review. South African Journal of Chemical Engineering. 2024 Oct 1;50(1):261-80.

[40] Zhao T, Gu C, Qi J, Liu J, Wang Y, Chen X, Guo F, Li Y. In vitro and in vivo performance of amorphous solid dispersions of ursolic acid as a function of polymer type and excipient addition. Journal of Pharmacy and Pharmacology. 2024 Dec;76(12):1584-98.

[41] Prakash S. Nano-based drug delivery system for therapeutics: a comprehensive review. Biomedical Physics & Engineering Express. 2023 Sep 1;9(5):052002.

[42] Wal P, Kaushal S, Dwivedi J, Patel P, Sachan P, Srivastava P. Multifunctional roles and phytopharmacological potential of ursolic acid:

an invaluable natural nutraceutical agent. Russian Journal of Bioorganic Chemistry. 2025 Feb;51(1):1-34.

[43] Pironi AM, de Araújo PR, Fernandes MA, Salgado HR, Chorilli M. Characteristics, biological properties and analytical methods of ursolic acid: A review. Critical reviews in analytical chemistry. 2018 Jan 2;48(1):86-93.

[44] Maghsoudi S, Taghavi Shahraki B, Rabiee N, Fatahi Y, Dinarvand R, Tavakolizadeh M, Ahmadi S, Rabiee M, Bagherzadeh M, Pourjavadi A, Farhadnejad H. Burgeoning polymer nano blends for improved controlled drug release: a review. International Journal of Nanomedicine. 2020 Jun 19:4363-92.

[45] Sharma N, Kumar P, Singh S, Agarwal G, Gupta S. Insights into the Recent Breakthroughs in Nanotechnological Outlook of Pentacyclic Triterpenoids: An Updated Approach. Current Pharmaceutical Design. 2026.

[46] Maghsoudnia N, Eftekhari RB, Sohi AN, Zamzami A, Dorkoosh FA. Application of nano-based systems for drug delivery and targeting: a review. Journal of Nanoparticle Research. 2020 Aug;22(8):245.

[47] Yu D, Kan Z, Shan F, Zang J, Zhou J. Triple strategies to improve oral bioavailability by fabricating coamorphous forms of ursolic acid with piperine: enhancing water-solubility, permeability, and inhibiting cytochrome P450 isozymes. Molecular Pharmaceutics. 2020 Sep 14;17(12):4443-62.

[48] Patne AY, Akramuddaula K, Patel D, Suryawanshi M, Vinchurkar K. Applications of natural polymers in controlled-release systems. InInnovative Pharmaceutical Excipients: Natural Sources 2025 Jul 29 (pp. 249-298). Singapore: Springer Nature Singapore.

[49] Zhou G, Liu H. Commercial Translation of Electrochemical Biosensors: Supply Chain Strategy, Scale-Up Manufacturing, and Regulatory–Quality Considerations. Biosensors. 2026 Feb 9;16(2):112.

[50] Bernard M, Jubeli E, Pungente MD, Yagoubi N. Biocompatibility of polymer-based biomaterials and medical devices–regulations, in vitro screening and risk-management. Biomaterials science. 2018;6(8):2025-53.

[51] Miastkowska M, Kulawik-Pióro A, Lasoń E, Śliwa K, Malinowska MA, Sikora E, Kantyka T, Bielecka E, Maksylewicz A, Klimaszewska E, Ogorzałek M. Topical formulations based on ursolic acid-loaded nanoemulgel with potential application in psoriasis treatment. Pharmaceutics. 2023 Oct 31;15(11):2559.

[52] Ji G, Li Y, Zhang Z, Li H, Sun P. Recent advances of novel targeted drug delivery systems based on natural medicine monomers against hepatocellular carcinoma. Heliyon. 2024 Jan 30;10(2).

[53] Car J, Tan WS, Huang Z, Sloot P, Franklin BD. eHealth in the future of medications management: personalisation, monitoring and adherence. BMC medicine. 2017 Apr 5;15(1):73.

[54] Poudel K, Gautam M, Maharjan S, Jeong JH, Choi HG, Khan GM, Yong CS, Kim JO. Dual stimuli-responsive ursolic acid-embedded nanophytoliposome for targeted antitumor therapy. International Journal of Pharmaceutics. 2020 May 30; 582:119330.

[55] Khopade AJ, Shah M. Challenges for commercial translation of nanomedicines: from lab scale to production scale. InCommercial scale production of nanomedicines 2025 (pp. 1-40). CRC Press.

[56] Najafi F, Farrokhzad N, Ghaemi A, Khezri DA, Hajiabbas M, Khanizadeh A, Farsani NK, Khoramipour M, Fatemipayam N, Zadeh ES, Goodarzi A. Advancement in nanocarrier-mediated delivery of herbal bioactives: from bench to beside. Natural Products and Bioprospecting. 2025 Dec;15(1):1-54.

[57] Mlala S, Oyedeji AO, Gondwe M, Oyedeji OO. Ursolic acid and its derivatives as bioactive agents. Molecules. 2019 Jul 29;24(15):2751.

[58] Kamaly N, Yameen B, Wu J, Farokhzad OC. Degradable controlled-release polymers and polymeric nanoparticles: mechanisms of controlling drug release. Chemical reviews. 2016 Feb 24;116(4):2602-63.

[59] Ren J, Lin H, Zhang Y, Li X, Zhang Z, You C, Wang F. The chitosan/cellulose nanocrystal cross-linked carriers effectively encapsulate ursolic acid to enhance the delivery of bioactive natural products. Journal of Drug Delivery Science and Technology. 2024 Aug 1; 97:105687.

[60] Abdeltawab H, Svirskis D, Sharma M.Formulation strategies to modulate drug

release from poloxamer based in situ gelling systems. Expert Opinion on Drug Delivery. 2020 Apr 2;17(4):495-509.

[61] Bagade O, Doke P. Lipid and Polymer Based Nano-Phytotherapeutics. Nanofabrication. 2023; 8:1773.