List of 10 best papers

1. **Waghule T**, Saha RN, Alexander A, Singhvi G. Tailoring the multi-functional properties of phospholipids for simple to complex self-assemblies. Journal of Controlled Release. 2022 Sep 1;349:460-74.

Impact factor: 11.46

Highlights: This review focuses on the relationship between the structural features of a phospholipid molecule and the formation of different lipid-based nanocarrier drug delivery systems. Various factors affecting the self-assembly of different phospholipids into distinct structures are summarized in this review. Finally, relevant recent case studies covering different types of phospholipid-based systems including simple to complex assemblies are referred. Different carriers in the size range of 50 nm to a few microns can be prepared using phospholipids which can be delivered either through oral, intravenous, nasal, dermal, transmucosal, or subcutaneous routes. The role of phospholipids as solubilizer, emulsifier, surfactant, permeation enhancer, coating agent, release modifier, and liposome former were explored through recent advancements in research. The information can guide the formulation scientist in selection of appropriate phospholipids while designing a drug delivery system.

2. **Waghule T**, Singhvi G, Dubey SK, Pandey MM, Gupta G, Singh M, Dua K. Microneedles: A smart approach and increasing potential for transdermal drug delivery system. Biomedicine & pharmacotherapy. 2019 Jan 1;109:1249-58.

Impact factor: 7.419

Highlights: The effect of most of the therapeutic agents is limited due to the stratum corneum layer of the skin, which serves as a barrier for the molecules and thus only a few molecules are able to reach the site of action. This review describes the various potential and applications of the microneedles in comparison to hypodermic needles, topical creams, and transdermal patches. The various types of microneedles like solid, dissolving, hydrogel, coated and hollow microneedles; and the fabrication methods are discussed through recent case studies. This system has increased its application to many fields like oligonucleotide delivery, vaccine delivery, insulin delivery, and even in cosmetics.

3. **Waghule T**, Swetha KL, Roy A, Saha RN, Singhvi G. Exploring temozolomide encapsulated PEGylated liposomes and lyotropic liquid crystals for effective treatment of glioblastoma: in-vitro, cell line, and pharmacokinetic studies. European Journal of Pharmaceutics and Biopharmaceutics. 2023 May 1;186:18-29.

Impact factor: 5.589

Highlights: Temozolomide (TMZ) is one of the best choices for treating glioblastoma. However, due to the short plasma half-life, only 20–30 % brain bioavailability can be achieved using

traditional formulations. In the present study, PEGylated liposomes and lyotropic liquid crystals (LLCs) were developed and investigated to prolong the plasma circulation time of TMZ. Industrially feasible membrane extrusion and modified hot melt emulsification techniques were utilized during the formulation. Liposomes and LLCs in the particle size range of 80–120 nm were obtained. The nanocarriers were found to show a prolonged release of up to 72 h. The cytotoxicity studies in glioblastoma cell lines revealed a ~1.6-fold increased cytotoxicity compared to free TMZ. PEGylated liposomes and PEGylated LLCs were found to show a 3.47 and 3.18-fold less cell uptake in macrophage cell lines than uncoated liposomes and LLCs, respectively. A 1.25 and 2-fold increase in the plasma $t_{1/2}$ was observed with PEGylated liposomes and PEGylated LLCs, respectively, compared to the TMZ when administered intravenously. Extending plasma circulation time of TMZ led to significant increase in brain bioavailability. Overall, the observed improved pharmacokinetics and biodistribution of TMZ revealed the potential of these PEGylated nanocarriers in the efficient treatment of glioblastoma.

4. **Waghule T**, Swetha KL, Roy A, Saha RN, Singhvi G. Quality by design assisted optimization of temozolomide loaded PEGylated lyotropic liquid crystals: Investigating various formulation and process variables along with in-vitro characterization. Journal of Molecular Liquids. 2022 Apr 15;352:118724.

Impact factor: 6.633

Highlights: The objective of the present study was to develop and characterize TMZ loaded lyotropic liquid crystals (LLCs) for intravenous delivery. Various formulation and process variables were studied in detail, following the quality by design principles. A three-level Box Behnken design was used for optimization. The effect of lipid concentration, surfactant concentration, and co-surfactant concentration on response variables like size, size distribution, zeta potential, entrapment efficiency, and drug loading was investigated using the statistical data obtained by Design Expert_ software. The results demonstrated that LLCs were obtained in the size range of 53.15–186.50 nm with PDI less than 0.25. TMZ loaded LLCs were found to follow Korsmeyer's Peppas model and showed sustained release up to 72 h. PEGylated LLCs showed less than 5% hemolysis. The results revealed that the prepared LLCs could be a potential delivery system to enhance the efficacy of TMZ. Additionally, the preparation method involved a minimum number of steps ensuring reproducibility and scalability.

5. **Waghule T**, Saha RN, Singhvi G. Exploring microfluidics and membrane extrusion for the formulation of temozolomide-loaded liposomes: investigating the effect of formulation and process variables. Journal of liposome research. 2023 Apr 3;33(2):170-82.

Impact factor: 5.586

Highlights: The present research study selected an amphiphilic drug Temozolomide (TMZ). It has a short half-life in the plasma due to its pH-dependent stability. Various critical and non-critical

parameters affecting the critical quality attributes were identified and studied using risk-based assessment. The effect of various material attributes and process parameters on the critical quality attributes of the temozolomide-loaded liposomes prepared by microfluidics and membrane extrusion techniques were investigated in detail. Liposomes in the size range of 100–150nm were targeted. Both techniques were optimized with a minimum number of critical process parameters. The obtained information will be beneficial to formulation scientists for designing liposomes for an amphiphilic drug on a large scale.

6. **Waghule T**, Dabholkar N, Gorantla S, Rapalli VK, Saha RN, Singhvi G. Quality by design (QbD) in the formulation and optimization of liquid crystalline nanoparticles (LCNPs): A risk based industrial approach. Biomedicine & Pharmacotherapy. 2021 Sep 1;141:111940.

Impact factor: 7.419

Highlights: Quality by Design (QbD) is a systematic method that can be utilized in formulation development. In this work, the application of QbD in the formulation of liquid crystalline nanoparticles (LCNPs) has been explored. The elements of QbD, viz. quality target product profile, critical quality attributes, critical material attributes, critical process parameters, quality risk management, design of experiments, and control strategy for the development of LCNPs have been explained in-depth with case studies. The present work will help the reader to understand the nitty-gritties in the application of QbD in the formulation of LCNPs, and provide a base for QbD-driven formulation of LCNPs with a regulatory perspective (better product and process understanding, the flexibility of process within the design space, implementation of more effective and efficient control strategies, easy transfer from bench to bedside, and more robust product)

7. **Waghule T**, Rapalli VK, Singhvi G, Gorantla S, Khosa A, Dubey SK, Saha RN. Design of temozolomide-loaded proliposomes and lipid crystal nanoparticles with industrial feasible approaches: comparative assessment of drug loading, entrapment efficiency, and stability at plasma pH. Journal of Liposome Research. 2021 Apr 3;31(2):158-68.

Impact factor: 5.586

Highlights: The objective of this work was to formulate lipid-based drug delivery systems to enhance the brain bioavailability by prolonging the drug release and circulation time of the Temozolomide to overcome the limitations of the existing therapies and possible reduction of side effects. The size of the nanocarriers obtained was less than 300nm and the PDI obtained was less than 0.3. The designed formulation showed higher entrapment efficiency as compared to the other reported nanocarriers of temozolomide. The designed formulations showed prolonged drug release from 12 to 20 h compared to 6 h for the pure drug. About 95% of the pure drug was degraded at plasma pH at the end of 12 h, whereas only 68% and 77% was degraded when entrapped inside the lipid crystal nanoparticles and proliposomes respectively.

8. **Waghule T**, Saha RN, Singhvi G. UV spectroscopic method for estimation of temozolomide: Application in stability studies in simulated plasma pH, degradation rate kinetics, formulation design, and selection of dissolution media. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2021 Sep 5;258:119848.

Impact factor: 4.831

Highlights: In this research study, analytical methods were developed for the estimation of Temozolomide (TMZ) using two media pH 1.2 (0.1 N HCl) and pH 4.5 acetate buffer, which were validated for linearity, range, precision, accuracy, limit of detection, limit of quantification, and specificity as per ICH guidelines. The % RSD was found to be <2% indicating the reliability of the method. Further, the application of the developed methods was explored. The stability of TMZ in three pH conditions (1.2, 4.5, and 7.4) and the respective degradation rate kinetics was studied. Conversion of TMZ was found to follow first order kinetics with the conversion rate of 0.0011, 0.0011, and 0.0453 h_1 in pH 1.2, 4.5, and 7.4 respectively. The developed methods accurately estimated the TMZ concentration in lipid nanoformulation (liposomes) indicated by ~100% recovery. The developed methods were found to be suitable for routine analysis, for the determination of drug stability and estimation of temozolomide in lipid nanoformulations.

9. **Waghule T**, Gorantla S, Rapalli VK, Shah P, Dubey SK, Saha RN, Singhvi G. Emerging trends in topical delivery of curcumin through lipid nanocarriers: effectiveness in skin disorders. AAPS PharmSciTech. 2020 Oct;21:1-2.

Impact factor: 4.026

Highlights: Curcumin has been reported to act on diverse molecular targets like receptors, enzymes, and co-factors; regulate different cellular signaling pathways; and modulate gene expression. The topical delivery of curcumin seems to be more advantageous in providing a localized effect in skin diseases. However, its low aqueous solubility, poor skin permeation, and degradation hinder its application for commercial use despite its enormous potential. Lipid-based nanocarrier systems including liposomes, niosomes, solid lipid nanoparticles, nanostructured lipid carriers, lyotropic liquid crystal nanoparticles, lipospheres, and lipid nanocapsules have found potential as carriers to overcome the issues associated with conventional topical dosage forms. Nano-size, lipophilic nature, viscoelastic properties, and occlusive effect of lipid nanocarriers provide high drug loading, hydration of skin, stability, enhanced permeation through the stratum corneum, and slow release of curcumin in the targeted skin layers. This review particularly focuses on the application of lipid nanocarriers for the topical delivery of curcumin in the treatment of various skin diseases. Furthermore, preclinical studies and patents have also indicated the emerging commercialization potential of curcumin-loaded lipid nanocarriers for effective drug delivery in skin disorders.

10. **Waghule T**, Patil S, Rapalli VK, Girdhar V, Gorantla S, Kumar Dubey S, Saha RN, Singhvi G. Improved skin-permeated diclofenac-loaded lyotropic liquid crystal nanoparticles: QbD-driven industrial feasible process and assessment of skin deposition. Liquid crystals. 2021 May 28;48(7):991-1009.

Impact factor: 2.676

Highlights: The purpose of the present study was to optimise diclofenac diethylamine-loaded liquid crystal nanoparticles (LCNPs) using the principles of quality by design. Based on risk assessment, the effect of various formulation variables on the critical quality attributes was investigated. A three-level Box-Behnken design with 14 runs was utilised for optimisation. The LCNPs were evaluated for size, polydispersity index, zeta potential, entrapment efficiency, morphology, solid-state characterisation, and drug release. The LCNPs were found to show prolonged drug release up to 12 h as compared to the free drug which showed a 100% release in less than 3 h. The optimized formulation was further investigated for scale-up studies, incorporated into carbopol gel and characterised for rheological parameters, skin permeation, and skin accumulation. Ex-vivo skin permeation studies revealed 1.55 times more permeation as compared to the marketed formulation. The designed gel had the potential to prolong the drug release, improve the permeation of drug through the skin layers, and industrial feasibility.