ejpmr, 2025, 12(9), 01-07

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

SJIF Impact Factor 7.065

Review Article

ISSN (O): 2394-3211

ISSN (P): 3051-2573

REVIEW ON NOVEL HERBAL DRUG DELIVERY SYSTEM USED IN DIABETIC MELLITUS

Sandip T. Thoke[1*], Swapnil B. Deshmukh[1], Umesh T. Jadhao[2], Dr. R. D. Wagh[1], Mr. T.A. Shaikh[1]

[1]Dcs's A.R.A. College of Pharmacy, Nagaon, Dhule Maharashtra- 424 005, India.
[2]SVP College of Pharmacy Hatta Tq. Basmath Dist. Hingoli, Maharashtra.

***Corresponding Author: Sandip T. Thoke**

Dcs's A.R.A. College of Pharmacy, Nagaon, Dhule Maharashtra- 424 005, India.

Article Received on 02/07/2025 **Article Revised on 22/07/2025** **Article Accepted on 12/08/2025**

ABSTRACT

Diabetes mellitus is a chronic metabolic disorder characterized by high blood glucose levels due to insulin deficiency or resistance. Traditional treatments often involve synthetic drugs, which can have side effects and long-term health implications. The integration of novel drug delivery systems with herbal medicines offers a promising approach for the management of diabetes mellitus. The novel herbal drug delivery systems included Liposomes, Phytosomes, Niosomes, Ethosomes, Proniosomes, Transferosomes, Microsphere, Nanoparticles. etc. These advanced delivery systems improve the bioavailability, stability, and efficacy of herbal compounds, providing a safer and more effective alternative to conventional diabetes treatments. Continued research and development in this field hold the potential to revolutionize diabetes care and improve patient outcomes.

KEYWORDS: Transferosomes, Phytosome, Bioavailability, Diabetes Mellitus, Novel Drug Delivery Systems.

INTRODUCTION

Diabetes mellitus (DM) is a glucose metabolism disease characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Type 1 (T1) DM results from an absolute deficiency in insulin caused by the failure of secretion by the pancreas.[1] while type 2 (T2) DM is characterized by insulin resistance and relative insulin deficiency.[2] Gestational diabetes mellitus (GDM) is diagnosed in the second or third trimester of pregnancy in women without a previous history of DM.[3] Primary prevention is the main aim at preventing diabetes from occurring in susceptible individuals or in general population.[4] Diabetes Mellitus can lead to serious complications over time if not properly managed, such as cardiovascular disease, kidney damage, nerve damage (neuropathy), and eye damage (retinopathy).[5] Insulin replacement therapy is the mainstay for patients with type 1 DM while diet and lifestyle modifications are considered the cornerstone for the treatment and management of type 2 DM.[6] Traditional treatments often involve synthetic drugs, which can have side effects and long-term health implications.(Table-01) In the past few decades, considerable attention has been concentrated on the evolution of a novel drug delivery system (NDDS) for herbal drugs.[7] Herbal medicine includes herbs, plant materials, herbal preparations and herbal finished products containing active ingredients that are plant parts, or ingredients. Other botanical materials, or combinations, and specially used for the prevention and treatment of diseases.[8] While herbal medicines offer many benefits, they also present challenges such as poor solubility, low bioavailability, and instability. These challenges necessitate innovative drug delivery systems to enhance their therapeutic efficacy.[9] (Fig.2)

Types Novel Herbal Drug Delivery Systems

Several approaches in case of new herbal drug delivery system include different types of expressions such as liposomes, phytosomes, pharmacosomes, museums, nanoparticles, microspheres, transfersomes, ethosomes, transdermal drug delivery system (TDDS), and proniosomes etc.[10] (fig.01)

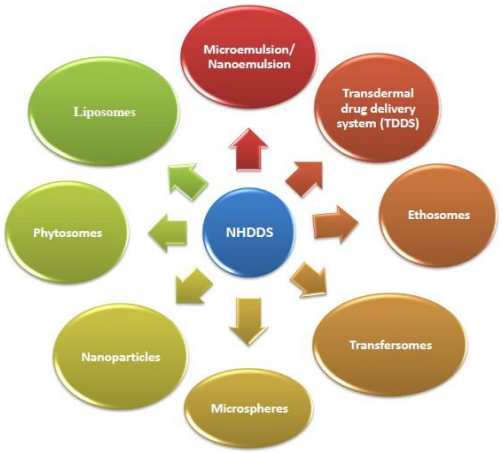

Table -01: Antidiabetic drugs in conventional formulations.[12]

S. No.	Drug/formulation	Indication	Trade name	Manufacturer
1	Insulin injections	T1DM and T2DM	Lantus	Sanofi Aventis
			Humulin & Huminsulin	Eli Lilly
			Insugen (Biocon)	Biocon
			Wosulin (Wockhardt)	Wockhardt
			Insuman (Sanofi Aventis)	Sanofi Aventis
2	Metformin tablets	Gestational & T2DM, Polycystic syndrome	Glucophage	Bristol Myers Squibb
			Riomet	Ranbaxy
			Obimet	Abbott
			Gluformin	AHPL
3	Glimepiride tablets	T2DM	Amaryl	Sanofi Aventis
			Glimy	Shrrishti HC
			Orinase	CCL
			Glimpid	Ranbaxy Lab.
4	Glibenclamide tablets	T2DM	Daonil&Semi-Daonil	Sanofi Aventis
			Euglucon	AHPL
5	Glipizide tablets	T2DM	Glynase	USV
			Glucotrol	Jenburkt
6	Gliclazide tablets	T2DM	Glizid	Panacea
			Glyloc	Cadila
			Reclide	Dr. Reddy's
7	Rosiglitazone tablets	T2DM	Avandia	Glaxo Smith Kline
8	Miglitol tablets	T2DM	Glyset	Pharmacia and Upjohn Company
9	Repaglinide tablets	T2DM	Prandin	Novo Nordisk INC
10	Acarbose tablets	T2DM	Glucobay	Bayer
			Precose	Genovate
11	Glibenclamide + Metformin tablets	Gestational & T2DM,	Aviglen Forte & Aviglen-MF	Avinash
		Polycystic syndrome	BEN-Q-MET	Q Check
			Benclamet	RPG LS
12	Rosiglitazone + Metformin tablets	T2 & Gestational DM	Avandamet	Glaxo Smith Kline
13	Rosiglitazone + Glimepiride tablets	T2DM	Avandaryl	Glaxo Smith Kline
14	Liraglutide injection	T2DM	Victoza	Novo Nordisk
15	Exenatide injection	T2DM	Exapride	Sun pharma

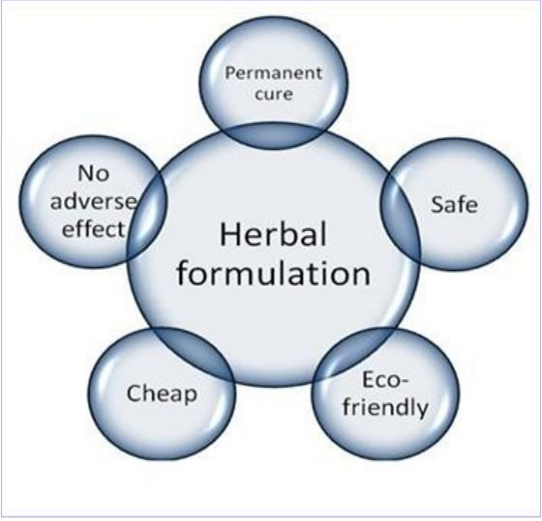

Figure 2: Pictorial representation of NHDDSs used for the delivery of Antidiabetics.[13]

Liposomes

The spherical liposomes include a portion of the solvents, which is allowed to freely permeate (float) into their core. Condensed phospholipid bilayers vesicles with an entirely confined aqueous volume are called liposomes.[14] A lipid membrane bi-layer made primarily by phospholipids, whether they are organic or manufactured. The Head Greek terms "Lipos," which represents fat, and "Soma," which denotes flesh, are the origin of the phrase "liposome.[15] Liposomes can be classified on the basis of size and number of bilayers. They are classified as multilamellar vesicles (MLV), large unilamellar vesicles (LUV) and small unilamellar vesicles (SUV).[16] A variety of herbal liposomal formulations have been reported for herbal drugs where liposome are able to enhance product performance by solubility enhancement, improving bioavailability, targeting at site of action and prolonged release of drug.[18]

Method of preperation of liposomes

- Thin film hydration method. (Bangham method)
- Reverse-phase evaporation method.
- Solvent injection methods.
- Detergent removal method.
- Dehydration-rehydration method.
- Heating method.
- Ph jumping method.
- Microfluidic channel method.
- Supercritical fluidic method.[20]

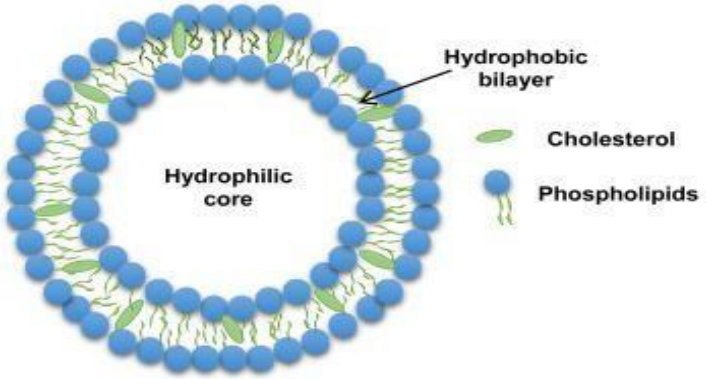

Figure 3. Schematic representation of liposomes.[17]

Table 2: Liposomal herbal formulations and their applications.[19]

Name of BioactiveComponent/ Plant	Application
Essential oil from *Atractylodesmacrocephala Koidz*	Increase in solubility and bioavailability
Essential oil of *O. dictamnus*	Increase in activity
Extracts of *Tripterygium wilfordi*	Reduction in side effects
Quercetin	Increase in bioavailability andreduction in side effects
Silymarin extract	Increase in hepatoprotective activity
Essential oil of *Artemisia arborescens L.*	Increase in stability
Capsaicin	Increase in permeation as prolongation of action
Taxanes	Decrease in toxicity

Phytosomes

Phytosome is a complex of phospholipids and natural active ingredients. Phytosome increases absorption of herbal extract when applied topically or taken orally.[21] Phytosomes differs from liposomes, in phytosomes phytoconstituents and phospholipids are present in1:1 or 1:2 ratio whereas in liposomes water soluble constituents is surrounded by several phosphatidyl choline units. Phytosomes are lipophilic vesicular drug delivery system with definite melting point, these are freely soluble in non-polar solvents and moderately soluble in fats (Figure 4).[23]

Table 3: Phytosomes herbal formulations and their applications.[22]

Name of Bioactive component / plant	Apllication
Ginseng -Ginsenosides	Increase absorption
Green tea -Epigallocatechin	Increase absorption
Curcumin- Curcumin	Increase Bioavabiliaty

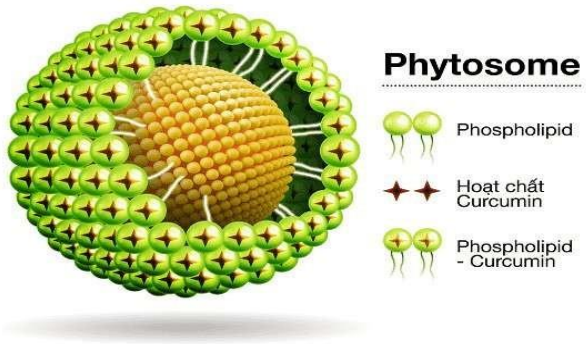

Figure 4: structure of Phytosome.[24]

Method of preperation of phytosomes

- Solvent evaporation/thin film hydration method
- Anti-solvent precipitation
- Freeze drying or lyophilization.[25]

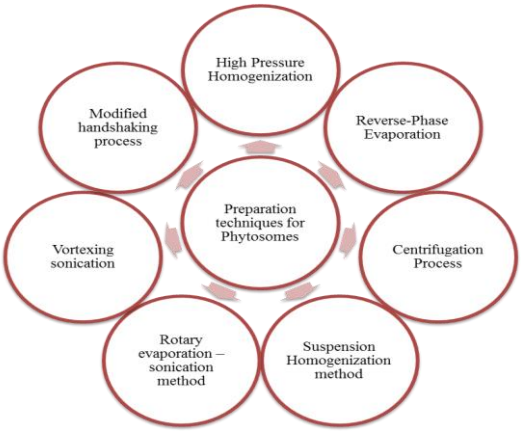

Figure 5: Methods of preparation of phytosome.[26]

Ethosome

The Ethosomes are non-invasive carriers that allow medicinal products to enter deep skin layers and systemic circulation. Ethosomes are soft vesicles customized to improve the delivery of active agents, such as drugs and natural products. They are primarily composed of phospholipids (phosphatidylserine, phosphatidylcholine, and phosphatidic acid), high ethanol concentrations, and deionized water.[27] The high concentration of ethanol makes ethosomes the best choice for skin due to impairment of the skin lipid bilayer. Thus, when ethanol is incorporated into the vesicle membrane, it provides the ability to reach vesicles to the stratum corneum. Therefore, these soft vesicles serve as new vesicular carriers for improved skin delivery. The size of ethosomes may be modified from nanometers to micrometers. Ethosomes have been found to be significantly superior in the quantity and depth of drugs delivered through the skin compared to liposomes and many other commercial transdermal and dermal delivery platforms.[28,31]

Methods of Preparation of Ethosomes

- Hot method
- Cold method
- Classic Mechanical Dispersion Method.[32]

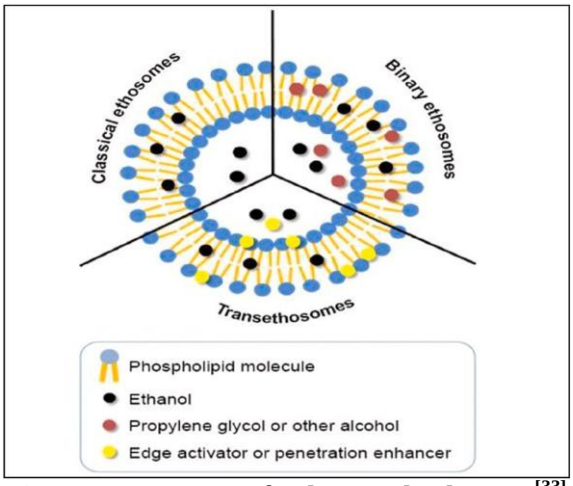

Figure: 6. structure of Ethosomal subtypes.[33]

Nanoparticles (NPs)

Enhance the solubility and stability of herbal compounds. For example, curcumin nanoparticles have shown improved bioavailability and glucose-lowering effects.[31] Nanoparticles are particles between 1 and 100 nanometers in size. In nanotechnology, a particle is defined as a small object that behaves as a whole unit with respect to its transport and properties. Particles are further classified according to diameter.[34] [Figure 7]

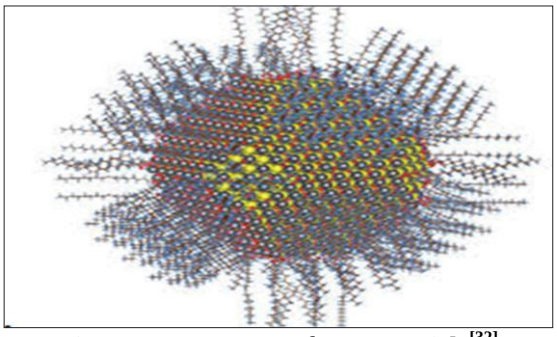

Figure: 7. Structure of Nanoparticle[32]

Types of Nanoparticles

Inorganic nanoparticles- The various types of inorganic particles, namely, magnetic, metallic, ceramic and nanoshells, their description, size.

Organic nanoparticles- The various types of organic nanoparticles, namely, carbon nanotubes, quantum dots, dendrimers, liposome and polymers, their description and size.

Methods of Preparation of Nanoparticles

- High-pressure homogenization method
- Solvent emulsification-diffusion method
- Salting-out method.[35-36]

Transfersomes

Transferosomes are vesicular carrier systems that are specially designed to have at least one inner aqueous compartment that is enclosed by a lipid bilayer, together with an edge activator.[37] (Figure 8)

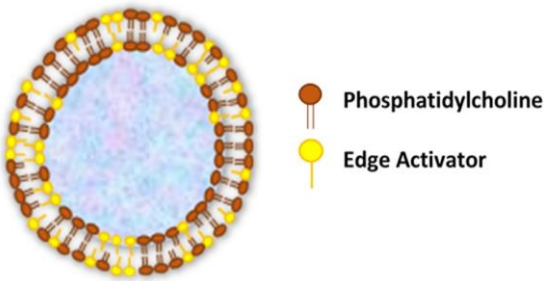

Figure1: Structure of transfersomes.[38]

Preparation Methods

- Thin Film Hydration Technique/Rotary Evaporation-Sonication Method
- Vortexing-Sonication Method
- Modified Handshaking Process
- Suspension Homogenization Method
- Centrifugation Process
- Centrifugation Process
- Ethanol Injection Method.[39-40]

Microphere

Polymeric delivery devices called microsponges are made of porous microspheres. They are small, spherical particles that resemble sponges and have a highly porous surface.[38] They have less side effects and better patient compliance while also being very efficacious, stable, non-irritating, non-toxic, nonallergic, and non-mutagenic.[41]

Types of Microsphere

- Bioadhesive microspheres
- Magnetic microspheres
- Floating microspheres
- Radioactive microspheres
- Mucoadhesive microspheres.[42]

Formulation of Microsponges

- Liquid-Liquid suspension polymerization
- Quasi-emulsion solvent diffusion
- Drug Release Mechanism of Microsponges.[43]

Transdermal Patches

Deliver herbal drugs through the skin, bypassing the gastrointestinal tract and enhancing bioavailability. Transdermal patches containing green tea extract have shown potential in managing blood glucose levels.[44]

Hydrogels

Hydrogels have been defined as two or multicomponent systems consisting of a three-dimensional network of polymer chains and water that fills the space between macromolecules.[45] Three-dimensional polymer networks that can hold large amounts of water and encapsulate herbal extracts. Hydrogels loaded with aloe vera extract have shown sustained release and improved glucose control.[47]

CONCLUSION

The integration of novel drug delivery systems with herbal medicines offers a promising approach for the management of diabetes mellitus. These advanced delivery systems improve the bioavailability, stability, and efficacy of herbal compounds, providing a safer and more effective alternative to conventional diabetes treatments. Continued research and development in this field hold the potential to revolutionize diabetes care and improve patient outcomes.

REFERENCES

1. Ranjit Unnikrishnan, Ranjit Mohan Anjana, Viswanathan Mohan. A review on Diabetes mellitus and its complications in India. Nature Review, McMillan Publisher limited, 2016; 12: 357-370. www.https://doi:10.1038/nrendo.2016.53
2. Gao Y, Wang Y, Zhai X, He Y, Chen R, Zhou J, et al. Publication trends of research on diabetes mellitus and T cells (1997–2016): A 20-year bibliometric study. PLoS ONE, 2017; 12(9): e0184869. https://doi.org/10.1371/journal.pone.0184869.
3. Akram T Kharroubi, Hisham M Darwish. Review on Diabetes mellitus: The epidemic of the century. World J Diabetes, 2015; 6(6): 850-867. DOI: 10.4239/wjd.v6.i6.850.
4. Ross, R., Dagnone, D., Jones, P.J. Reduction in obesity and related co-morbid conditions after diet induced weight loss or exercise-induced weight loss in men. A randomized, controlled trial. Ann Int Med, 2000; 133: 92-103.
5. Bastaki, S., Review Diabetes mellitus and its treatment, Int J Diabetes & Metabolism, 2005; 13: 111-134.
6. Kumar, P.J., Clark, M. Textbook of Clinical Medicine. 2002, Pub: Saunders (London), Page 1099- 1121.
7. Aziz Ahmed, Mohd Shuaib, et al. Herbal Medicines and Recent Development on Novel Herbal Drug Delivery System. Indonesian Journal of Pharmaceutical and Clinical Research, 2023; 6(01): 13–024.
8. Mandal SC, Mandal M. Current status and future prospects of new drug delivery system. Pharm Times, 2010; 42: 13-6.
9. Galave RN, et al. Review on Novel Herbal Drug Delivery System. Journal of Pharmaceutics and Nanotechnology, 2023; 11: 01-10.
10. Sarangi MK, Padhi S. Novel herbal drug delivery system: An overview. Arch Med Health Sci, 2018; 6: 171-9.
11. Murti et al. A Review on Novel Herbal Drug Delivery System and its Application. Current Traditional Medicine, 2023; 9(2): 43-55.
12. Chen Y-C, Hsieh W-Y, Lee W-F, et al. Effects of surface modi f ication of PLGA-PEG-PLGA nanoparticles on loperamide delivery efficiency across the blood–brain barrier. J Biomater Appl, 2013; 27(7): 909-922.

13. Hjorth S, Bengtsson H, Kullberg A, et al. Serotonin autoreceptor function and antidepressant drug action. J Psychopharmacol, 2000; 14(2): 177-185.
14. Chaturvedi M, et al. Recent development in novel drug delivery systems of herbal drugs. Int J Green Pharm, 2011; 5.
15. Abdallah MH, Sabry SA, Hasan AA. Enhancing transdermal delivery of glimepiride via entrapment in proniosomalgel. J Young Pharm. 2016; 8(4): 335-340.
16. Cheriyan P, et al. Formulation and characterization of maltodextrin based proniosomes of cephalosporins. Pharm.Sci, 2015; 3(1): 62-74.
17. Durgavati Yadav, Kumar Sandeep, Deepak Pandey, & Ranu Kumari dutta. Liposomes for Drug Delivery. Journal of Biotechnology & Biomaterials, 2017; 7(4): 276-283. DOI: 10.4172/2155-952X.1000276
18. Nsairat H, Khater D, Sayed U, Odeh F, Al Bawab A, Alshaer W. Liposomes: structure, composition, types, and clinical applications. Heliyon, 2022; 8(5): e09394. doi: 10.1016/j.heliyon.2022.e09394. PMID: 35600452; PMCID: PMC9118483.
19. Ashwani Goyal et al. Potential of Novel Drug Delivery Systems for Herbal Drugs. Ind J Pharm Edu Res, 2011; 45(3): 225-235.
20. Akanksha Zalke, et al. A Review: Novel Herbal Drug Delivery System. International Journal of Scientific Research in Engineering and Management, 2023; 7(5): 1-10. DOI: 10.55041/IJSREM21438
21. Anupama Singh, Phytosome: Drug Delivery System for Polyphenolic Phytoconstituents. Iranian Journal of Pharmaceutical Sciences Autumn, 2011; 7(4): 209-219.
22. Alka Verma, Kiran Sharma. Int. J. Pharm. Sci. Rev. Res., 2021; 69(2): 47-51.
23. Deepak S, Prashant U, Sukriti U. Phytosomes: An Advanced Drug Delivery System for Herbal Drug. Glob J Pharmaceu Sci, 2018; 6(1): 555679. DOI: 10.19080/GJPPS.2018.06.555679.
24. Rani M Londhe, et al. A Review on : Novel Herbal Drug Delivery System. Journal of Emerging Technologies and Innovative Research, 2022; 9(4): e546-e561.
25. Gaikwad et al. A review Overview of phytosomes in treating cancer: Advancement, challenges, and future outlook. Heliyon, 2023; 9: e1656 - e16571.
26. Sakure et al. Recent Trends and Future Prospects of Phytosomes: A Concise Review. Indian Journal of Pharmaceutical Sciences, 2024; 86(3): 772-790.
27. Singh, A. et al. LOX-1, the common therapeutic target in hypercholesterolemia: a new perspective of antiatherosclerotic action of aegeline, 2019; 8285730. doi:10.1155/2019/8285730. PMID: 31885819; PMCID: PMC6914969.
28. Anil Kumar .T, et al. A review on phytosomes as innovative delivery systems for phytochemicals. International Journal of Pharmacognosy and Chemistry, 2023; 4(1): 1-8.
29. Umesh Jadhao, Harshal Tare, Sachin K Jain., "Skin Penetrating Lipid Vesicles: Ethosomes in Drug Delivery and Cosmeceuticals" IJDDT, January - March 2024; 14(1): 496-505.
30. Umesh Jadhao, Harshal Tare "Formulation and Evaluation of Herbal Ethosomal Cream of Passiflora foetida Linn. For the Treatment of Psoriasis" IJDDT, January - March 2024; 14(1): 345-355. ISSN: 0975 4415
31. Umesh Jadhao, Harshal Tare., "Development and Evaluation Of Herbal Ethosomes Of Passiflora Foetida Linn For The Treatment Of Psoriasis" IJBPAS, October, Special Issue, 2023; 12(10): 535-549.
32. Poonam Verma, K. Pathak. Therapeutic and cosmeceutical potential of ethosomes: An overview. Journal of Advanced Pharmaceutical Technology & Research, 2010; 1(3): 274-282.
33. Chauhan, Neha.et al. Ethosomes: A novel drug carrier. Annals of Medicine & Surgery, 2022; 82: October 2022. | DOI: 10.1016/j.amsu.2022.104595
34. Bruna Vidal Bonifácio, et al. Nanotechnology-based drug delivery systems and herbal medicines: a review. International Journal of Nanomedicine, 2014; 9: 1–15.
35. Mamillapalli, et al.: Nanoparticles for herbal extracts. Asian Journal of Pharmaceutics, 2016; 10(2): S54.
36. Teja PK, et al. Herbal nanomedicines: Recent advancements, challenges, opportunities and regulatory overview. Phytomedicine, 2022; 96: 153890. doi:10.1016/j.phymed.2021.153890.
37. Yadav M, Bhatia VJ, Doshi G, Shastri K (2014) Novel techniques in herbal drug delivery systems. Int J Pharm Sci Rev Res, 28(2): 83–89.
38. Shree D, et al. Applications of Nanotechnology-mediated Herbal Nanosystems for Ophthalmic Drug. Pharm Nanotechnol, 2024; 12(3): 229-250. doi: 10.2174/2211738511666230816090046. PMID: 37587812.
39. Pradhan D, et al. Recent Advances in Herbal Nanomedicines for Cancer Treatment. Curr Mol Pharmacol, 2021; 14(3): 292-305. doi:10.2174/1874467213666200525010624. PMID: 32448111.
40. Shakthi Apsara Thejani, et al. Review on Transfersomes: A Promising Nanoencapsulation Technique for Transdermal Drug Delivery. Pharmaceutics, 2020; 12: 1-25. doi:10.3390/pharmaceutics12090855.
41. Jadhav Priyanka Vitthal, Rajasekaran S. Novel Approaches of Herbal Microsponges Design, Formulation and Characterization: An Overview. International Journal of Pharmaceutical Research and Applications, 2022; 7(5): 1280-1291.
42. Vikrant K, Nikam DR, Somwanshi SB, Gaware VM, Kotade KB, Dhamak KB, Khadse AN, Kashid VA. Microparticles: a novel approach to enhance the drug delivery-a review. IJPRD, 2011; 3(8): 170- 83.

43. Jain N, Sharma PK, Banik A. Recent advances in mirosponges drug delivery system. IJPSRR, 2011; 342: 13-4.
44. Mahesh Mangnale, et al. A Review on Microspheres: Method of Preparation and Evaluation. Ijppr. Human, 2021; 20(3): 485-497.
45. V.Arunachalam et al. Formulation And Evaluation of Herbal Transdermal Patches for Rheumatoid Arthritis. International Journal for Multidisciplinary Research, 2023; 5(6): 1-19.
46. Ahmed EM. Hydrogel: Preparation, characterization, and applications: A review. J Adv Res, 2015; 6: 105-21.
47. Prerna Thakur, et al. Preparation and evaluation of polyherbal hydrogels formulation for diabetic foot ulcer. Innovations in Pharmaceuticals and Pharmacotherapy, 2019; 7(3): 61-66.