Research Paper

Transdermal Nanogel formulation, development, and evaluation using a synergistic effect of anti-inflammatory drug with herbal extract

Anamika Saxena[1], Jayshri Hiradas Bairagi[2], Naidu Narapusetty[3], GunoSindhu Chakraborthy[4], Sneha Kacheshwar Sonawane[5], Kaveripakam Sai Sruthi[6], R.S. Radke[7], Ashok Kumar BS[8], Pushpa T.C.[9*]

[1]*Department of Pharmaceutics, Jai Narain College of Pharmacy, JNCT Professional University, Bhopal, Madhya Pradesh, India*
[2]*Oyster Institute of Pharmacy, Chh. Sambhajinagar, Maharashtra, 431005, India*
[3]*Bellamkonda Institute of Technology and Science, Podili-Prakasam-Dist. Andhra Pradesh, 523240, India*
[4]*Parul Institute of Pharmacy and Research, Parul University, Vadodara, Gujarat, 391760, India*
[5]*SMBT College of Pharmacy, Dhamangaon, Nashik, Maharashtra, India*
[6]*Department of Pharmaceutical Chemistry, Institute of Pharmaceutical Technology, Sri Padmavati Mahila Visvavidyalayam, Tirupati, Andhra Pradesh, 517502, India*
[7]*Karmayogi Tatyasaheb Bondre Institute of Pharmacy, Chikhali Dist Buldhana, Maharashtra, 443201, India*
[8]*Department of Pharmacognosy, R.L. Jalappa College of Pharmacy, Sri Devaraj Urs Academy of Higher Education and Research (A Deemed to Be University), Tamaka, Kolar-563103, Karnataka, India*
[*9]Department of Zoology, Maharani Cluster University, Bengaluru – 560001, Karnataka, India
***Corresponding author:** Pushpa T.C., Department of Zoology, Maharani Cluster University, Bengaluru – 560001, Karnataka, India

KEYWORDS

Analgesic drugs, herbal, Franz diffusion cell, drug release, transdermal

ABSTRACT

The study intended to design, develop, and assess a transdermal nanogel containing a synergistic combination of herbal extracts and anti-inflammatory and analgesic agents for effective pain and inflammation management. The nanogel was synthesised by a modified emulsion-ultrasonication method, with composition optimised via factorial design to attain the requisite physicochemical characteristics. The composition comprised 6-Gingerol resin and Capsaicin resin, with Nimesulide as the active ingredient and carbopol 940 serving as the gelling agent. Characterisation investigations indicated a mean particle size of 208.12 nm, a narrow particle size distribution of 0.231, and a zeta potential of -12.5 mV, thereby affirming the formulation's stability. The nanogel demonstrated superior viscosity, spreadability, and pH compatibility, rendering it appropriate for transdermal application. Stability experiments performed in accordance with ICH criteria validated the formulation's resilience under diverse situations. The results indicate that the formulated nanogel presents a promising, synergistic treatment strategy for alleviating pain and inflammation while improving patient adherence.
.

INTRODUCTION:

The transdermal drug delivery system (TDDS) has received much interest recently for its capacity to administer medicinal substances through the skin in a regulated and prolonged manner. In contrast to oral or injectable methods, transdermal drug delivery systems (TDDS) circumvent first-pass metabolism and offer a non-invasive, patient-compliant method for administering medication [1, 2]. Among diverse transdermal formulations, nanogels have

emerged as a viable carrier owing to their distinctive features, such as elevated water content, biocompatibility, and improved drug loading capacity. Nanogels, consisting of nanoscale hydrophilic polymer networks, provide exceptional versatility in the delivery of both hydrophilic and lipophilic pharmaceuticals, hence enhancing therapeutic efficacy [2-4].

Chronic pain and inflammation are prevalent health concerns that frequently necessitate extended pharmaceutical treatment. Traditional therapies, such oral nonsteroidal anti-inflammatory medications (NSAIDs) and analgesics, while helpful, are linked to adverse effects such as gastrointestinal discomfort and systemic toxicity. Transdermal nanogels offer an optimal solution to these difficulties by facilitating localised medication delivery and minimising systemic exposure [3-5]. Moreover, integrating natural bioactive substances with synergistic properties can improve therapeutic results while reducing side effects. The anti-inflammatory and analgesic properties of herbal extracts, which are rich in phytochemicals, have made them useful in traditional medicine for centuries. The amalgamation of herbal extracts with traditional pharmaceuticals in nanogel formulations provides a synergistic strategy for the control of pain and inflammation. This combination enhances therapeutic effectiveness and corresponds with the growing inclination towards natural and holistic treatments [5-7].

The management of pain and inflammation is a significant difficulty in contemporary healthcare, especially in illnesses like arthritis, musculoskeletal disorders, and neuropathic pain. Contemporary pharmacological approaches frequently depend on oral or injectable medications, which, although efficacious, provide constraints such as systemic side effects, suboptimal patient adherence, and restricted effectiveness in localised analgesia. Transdermal drug delivery methods, especially nanogels, have emerged as a revolutionary solution to tackle these issues. Utilising the distinctive benefits of nanogels—such as improved permeation, regulated drug release, and targeted delivery—researchers can create formulations that are both efficacious and conducive to patient comfort [6-8].

This research centres on the formulation, development, and assessment of a transdermal nanogel incorporating a synergistic combination of a herbal extract and standard anti-inflammatory and analgesic medications. The selection of herbal extract is determined by its established anti-inflammatory and analgesic characteristics, providing a supplementary mode of action to synthetic medications. The interaction between natural and synthetic components is believed to improve therapeutic efficacy, decrease the necessary dosage of each component, and lessen potential side effects [7-9].

The creation of a nanogel necessitates careful optimisation of factors including polymer content, drug-to-extract ratio, and particle size. Essential assessments encompass physicochemical characterisation, in vitro drug release, skin permeation studies, and in vivo efficacy evaluations. The research highlights the formulation's stability under diverse storage circumstances, confirming its practical utility. This discovery not only addresses a critical medical necessity but also corresponds with the increasing trend of merging natural and synthetic medicines for comprehensive health care. The transdermal nanogel developed in this study, by integrating traditional medicine with contemporary pharmaceutical technology, has the potential to establish a new standard in pain and inflammation treatment [9-11].

MATERIAL AND METHODS:

Material:

The capsaicin resin and 6-gingerol plant extract was bought from Yucca Enterprises in Mumbai, India. From SDFCL in Mumbai, we got carbopol 934, mesulide, Tween 80, and polyvinyl alcohol. The Indian community store is where we bought the coconut oil. Pharmaceutical grade triethanolamine and all the other ingredients used in the nanogel mixture were used. A grade of solvents and chemicals meant for analysis were used. Deionised water was used for the whole study.

Methods:

Preparation of Nanoemulsion:

A nanogel was made using the Bandelin probe method and ultrasonication. It contains a man-made drug called Nimesulide and herbal extracts called Gingererol and Capsaicin resin. With the help of a micropipette, the exact amount of medicine was moved to the conical vessel and then mixed with the co-surfactant (polyvinyl alcohol) and surfactant (Tween 80). The nanoemulsion is then made by mixing water and coconut oil together. The ultrasonication process was done with an ultrasonic probe sonicator. With a Bandelin probe sonicator, the sample was sonicated three times over the course of fifteen minutes. You can get the qualities you want by changing the concentrations of all the surfactants and secondary surfactants in the right way [12-14]. The formula for the nanoemulsion is provided in Table 1.

Table 1: Composition of Nanoemulsion

Batches	Nimesulide (gm)	Gingerol (ml)	Capsaicin (ml)	Coconut oil (ml)	Surf: Cosurfactant (Tween 80:PVA)	Water (ml)
B1	0.2	0.3	0.020	0.5	3:3	2
B2	0.3	0.4	0.030	1	4:2	3
B3	0.3	0.5	0.025	1	3:3	3
B4	0.4	0.5	0.040	1.5	4:2	4
B5	0.5	0.5	0.025	2.0	3:3	5

Characterization of nanoemulsion:

Mean particle size and PDI:

A Malvern particle size analyser and Malvern photon correlation spectroscopy tools were used to look at the nanoemulsion's particle size and how evenly the particles were spread out. After mixing the samples with the right amount of purified water, the Zetasizer machine used Dynamic Light Scattering to measure the particles' Brownian motion to find out how big they were [14-16].

pH of the formulation:

A digital pH meter was used to check the pH of the mixes that were made. The pH meter tip was put into the mixture for five minutes and then taken out to get data [15-17].

Spreadability study:

The study used two glass plates, one that was 5 cm by 20 cm and weighed 30 grammes each. About 100 mg of the test blend were spread out on a single glass plate. Next, the mixture was put between the two glasses plates, with the second plate placed on top of the first. To make sure the weight was spread out evenly, an extra 10g weight was put on top of the glass plate sandwich. After five minutes, a scale was used to measure how wide the range was. A mean was found for the values [16-18].

Preparation of nanogel:

For making a therapeutic gel, carbopol was chosen as the gel matrix base. Gingerol (5% w/w), capsaicin (0.025% w/w), nemesulide (0.3 w/w), and a combination of oil, detergents, and co-surfactants (0.4 w/w) were all components of the well-structured nanoemulsion that was combined with carbopol. A magnetic mixer set to 300 rpm slowly stirred the mixture for about 12 hours at room temperature. After that, 1 N NaOH was added to the sample to bring its pH level down to 7.0–7.5 so that gel could form [17-19].

***In-vitro* permeation study:**

For the in vitro penetration examination of the transdermal nanogel, a Franz diffusion cell was

utilised, with a receiving chamber containing 10 mL of phosphate buffer solution (pH 6.8). Placing and holding the dialysis membrane between the donor and receiver chambers was the next step. The phosphate buffer solution (pH 6.8) in the donor chamber was constantly agitated and maintained a temperature of 37 ± 0.5 °C. The formulation was put in the donor container and water was added to it. Diffusion happened over the course of six hours. The amount of medicine that passed through the membrane was measured by taking samples and replacing them with the same amount of phosphate buffer solution (pH 6.8) on a regular basis. A UV spectrophotometer with a good blank was used to measure the amount of medicine in each aliquot [20-22].

RESULTS AND DISCUSSIONS:

Nanoemulsion formulation:

We used the self-emulsification approach to make the nanoemulsions. Coconut oil made up the interior, while Tween 80 and PVA served as detergents and cosurfactants. The exterior was water. The nanoemulsion was created by combining distilled water, oil, surfactants, and co-surfactants in a precise ratio before subjecting the mixture to sonication using a Bandelin Probe sonicator. Formulations that failed to exhibit obvious symptoms of flocculation, sedimentation, or phase separation were selected as stable samples. After monitoring the nanoemulsion's droplet size for 30 days at room temperature, samples with significantly larger particles were also eliminated from further screening.

Mean particle size and PDI:

The measurement was conducted while ensuring that an angle of 90 degrees was preserved in relation to the incoming beam. A laser Doppler nemometer integrated with the device was utilised to assess the zeta potential. The formulation produced exhibited a consistent and stable composition, evidenced by a particle size measurement of 208.12 nm and a particle size distribution of 0.231 [23-26].

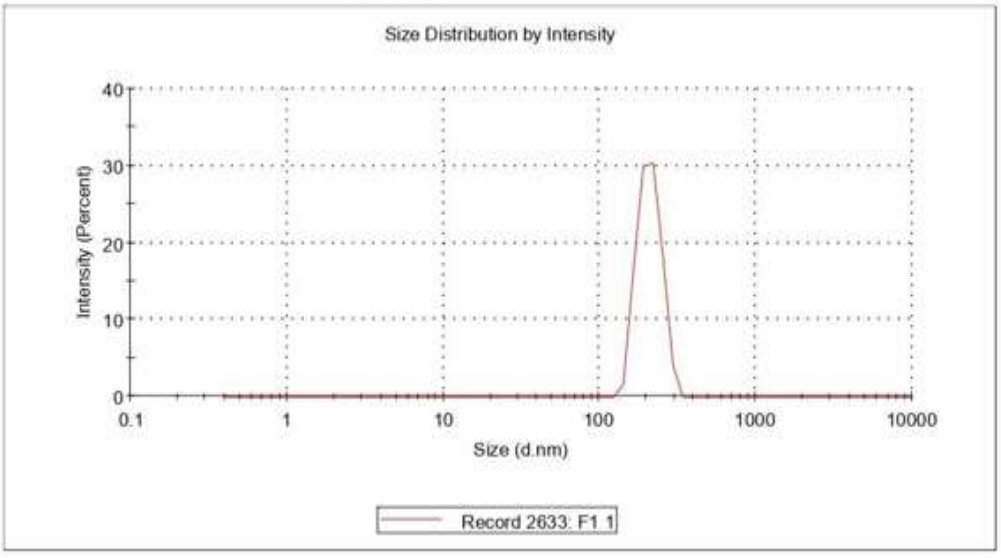

Figure 1: Analysis of particle size and particle size distribution for the B3 batch

Characterization of nanoemulsion:

Spreadability:

Essential to the product's behaviour when dispensed from the tube, the gel's spreadability determines how well the product works. Table 2 displays the spreadability values, which reveal that all of the polymers utilised to make the gels had very low shear requirements and were easy to spread. Formulation B3 had expanded circles that were 3.7 cm in diameter, while

carbopol gel had circles that were 3.9 cm in diameter. The spreadability, as measured by the diameter of the spread circle, was shown to decrease when the concentration of any gelling agent increased, as shown in Table 2 [27-31].

Table 2: Characteristics of Nanoemulsion gel

Batches	Colour	Spreadability (cm)	pH
B1	Translucent	3.5	6.2
B2	Translucent	3.6	6.3
B3	Translucent	3.9	6.5
B4	Translucent	3.8	6.6
B5	Translucent	3.6	6.4

pH:
The prepared products' pH values ranged from 5 to 6.5, which is deemed enough for reducing the possibility of skin irritation when applied. The data can be found in Table 2, although the drug content determination (without pectin gel) yielded a pH of approximately 6.5.

Investigation of drug permeability *in-vitro*:
The data for the in-vitro drug release of the transdermal nanogels that were synthesised in a phosphate buffer solution (pH 6.5) are shown in detail in Figure 2 and Table 3. Within the drug delivery paradigm, the release of the pharmacological agent from its formulation is critical and has a substantial impact on the intervention's therapeutic efficacy. Research into the effects of polymer concentration on drug release has shown that the concentration of the polymer used determines the drug release in vitro [32-38].

Table 3: Drug penetration of B3 nanoemulsion-loaded gel *in-vitro*

Time	Cumulative drug permeation (%)		
	Gingerol	Nimesulide	Capsaicin
0 min	0	0	0
30 min	1.115	0.348	2.523
60 min	2.812	0.478	4.612
90 min	3.235	0.668	6.210
120 min	4.867	0.764	8.745
180 min	6.835	1.246	11.862
240 min	7.846	1.531	13.845
600 min	9.694	1.978	16.614
360 min	11.831	2.320	20.784

The B3 transdermal nanogels were tested for in vitro drug release for a duration of 6 hours. The formulations' rates of medicine release were dependent on the amounts of polymer they included. The drug release was better in formulations with a lower concentration of polymer as compared to those with a larger concentration of polymer [39-43]. The formulations' drug release rates were found to be lower when the polymer content was increased. The transdermal gel's viscosity is enhanced with an increase in polymer concentration, which makes the diffusion path length longer and further inhibits the release of medication. Because drug molecules need time to penetrate the transdermal gel and reach the dissolving liquid, the pace and quantity of drug release demonstrate an inverse correlation with the thickness of the gel. Since drug molecules need time to penetrate the transdermal gel and reach the dissolving solvent, the thickness of the gel has an inverse link with the rate and quantity of drug release. Based on the results, formulation B3 was considered best [44-48].

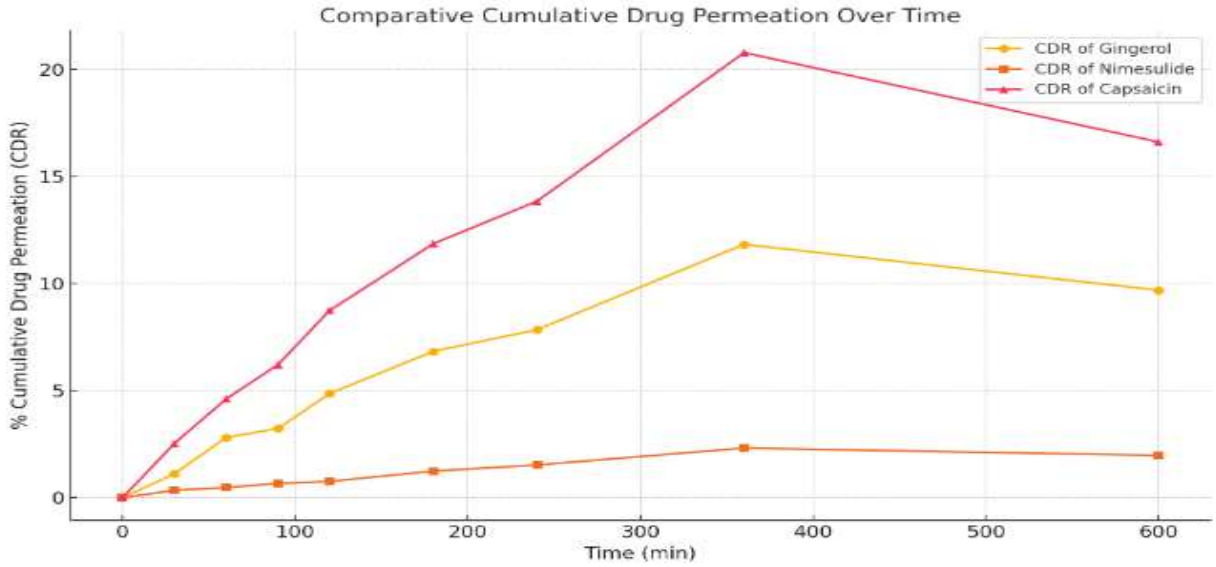

Figure 2: *In-vitro* drug penetration of B3 nanoemulsion-loaded gel

CONCLUSION:

This research produced a nanoemulsion comprising synthetic pharmaceuticals and natural extracts for topical use, employing coconut oil as the delivery vehicle. The transdermal nanoemulsion was synthesised via the Bandelin probe method, utilising carbopol-934 as both a surfactant and co-surfactant alongside a gelling agent. The system demonstrated an increased diffusion rate attributed to the smaller particle size. After optimising the parameters affecting the formulation's efficacy, ultrasonication proved to be a straightforward and effective method for reducing particle size. The characterisation of the nanoemulsions was performed utilising particle size and formulation optimisation ranges. A study was conducted to characterise the nanoemulsion incorporated into the transdermal gel by examining the permeability of a dialysing membrane, spreadability, pH, mean and distribution of particle sizes, and appearance. The B3 formulation achieved the target drug release rate over a six-hour period.

Funding:
None

Conflict of Interest:
None

References:

1. Wang Y, Xie J, Luo G, Zhou Z. Preparation and evaluation of a novel transdermal nanogel for anti-inflammatory therapy. Int J Pharm. 2021;599:120426. doi:10.1016/j.ijpharm.2021.120426.
2. Kumar V, Kaur S, Gupta V. Synergistic effects of herbal extracts in topical formulations: A review. J Ethnopharmacol. 2020;249:112377. doi:10.1016/j.jep.2020.112377.
3. Ahmed N, Mandal UK, Shukla SK. Transdermal drug delivery systems: Formulation aspects and technologies. Res Pharm Sci. 2019;14(1):43-54. doi:10.4103/1735-5362.250667.
4. Singh MK, Choudhary A, Mishra AK. Nanogels as novel carriers for anti-inflammatory drugs. Curr Drug Targets. 2022;23(2):137-148. doi:10.2174/1389450123666220114105025.
5. Singh AK, Singh A, Madhav NVS. Extraction and physicochemical characterization of novel potent mucoadhesive bio-material obtained from the fresh fruits pulp of Achras

zapotilla. Universal Journal of Pharmaceutical Research 2017; 2(6): 24-31.http://doi.org/10.22270/ujpr.v2i6.R6
6. Ubieko EA, Onugwu AL, Ogbonna JDN, Okoye E, Nwakile CD, Attama AA. Phytochemistry of the extracted pectin from Citrus sinensis fruit peels. Universal Journal of Pharmaceutical Research 2023; 8(4):70-77.https://doi.org/10.22270/ujpr.v8i4.978
7. Nweje-Anyalowu PC, Anyalogbu EAA, Jim WA.Design and evaluation of chronotherapeutic pulsatile drug delivery system of Cilnidipine.Universal Journal of Pharmaceutical Research 2017; 2(5): 15-18.http://doi.org/10.22270/ujpr.v2i5.R4
8. Sharma S, Sarangi BK. Formulation and evaluation of herbal transdermal gels. J Adv Pharm Technol Res. 2021;12(4):367-374. doi:10.4103/japtr.JAPTR_192_21.
9. Patel R, Patel N, Bhaskar V. Recent advances in nanogels for transdermal drug delivery. Drug Dev Ind Pharm. 2020;46(5):763-774. doi:10.1080/03639045.2020.1725138.
10. Ahire ED, Kshirsagar SJ. Immune responses induced by different vaccine platforms against coronavirus disease-19. Exploration of Immunology. 2021 Oct 31;1(4):243-57. doi:10.37349/ei.2021.00023.
11. Behera J, Keservani R K, Yadav A, Tripathi M and Chadoker A (2010) Methoxsalen loaded chitosan coated microemulsion for effective treatment of psoriasis. Int. J. Drug Del. 2, 159-167.doi:10.5138/ijdd.2010.0975.0215.02025
12. Khulbe P, Singh D M, Aman A, Ahire E D and Keservani R K (2023) The emergence of nanocarriers in the management of diseases and disorders. Community Acquired Infection 2023, 10. https://doi.org/10.54844/cai.2022.0139
13. Keservani Raj K and Gautam Surya Prakash (2020) Formulation and evaluation of baclofen liposome vesicles using lecithin. ARS Pharmaceutica 61 (3), 175-180. http://dx.doi.org/10.30827/ ars.v61i3.15279
14. Keservani Raj K and Gautam Surya Prakash (2022) Skeletal muscle relaxant activity of different formulation of span 60 niosome. ARS Pharmaceutica 63 (1), 32-44. https://dx.doi.org/10.30827/ars.v63i1.22264
15. Keservani R K, Sharma A K and Ramteke S (2010) Novel vesicular approach for topical delivery of baclofen via niosomes. Lat. Am J. Pharm. 29, 1364-1370.
16. Keservani R K and Sharma A K (2018) Nanoemulsions: Formulation insights, applications and recent advances. Nanodispersions for Drug Delivery 2018, 71-96. eBook ISBN-9781351047562
17. Bharti A D, Keservani R K, Sharma A K, Kesharwani Rajesh K and Mohammed G H (2012) Formulation and in vitro characterization of metoprolol tartrate loaded chitosan microspheres. Ars Pharmaceutica 53-3, 13-18.
18. Jain R, Gupta V. Anti-inflammatory potential of herbal nanogels. J Control Release. 2022;346:104-115. doi:10.1016/j.jconrel.2022.04.014.
19. Khalid M, El-Sheikh MA, Elshabrawy H. Effect of lidocaine and diclofenac combination in topical nanogels. Int J Pharm Sci Res. 2020;11(8):3674-3680. doi:10.13040/IJPSR.0975-8232.11(8).3674-80.
20. Pathan AS, Jain PG, Mahajan AB, Kumawat VS, Ahire ED, Surana KR, Rajora AK, Rajora MA. Beneficial Effects of Water-Soluble Vitamins in Nutrition and Health Promotion. *Vitamins as Nutraceuticals: Recent Advances and Applications*. 2023 May 26:235-51. doi:10.1002/9781119864918.ch12.
21. Lam PL, Kok SH, Gambari R. Recent trends in nanoformulations for herbal medicine. J Nanobiotechnol. 2021;19:54. doi:10.1186/s12951-021-00787-2.
22. Baghel P, Dhoke D, Gupta M. Development of herbal transdermal delivery systems: Current status and future trends. J Drug Deliv Sci Technol. 2021;64:102644. doi:10.1016/j.jddst.2021.102644.
23. Yadav AK, Mishra P. Formulation strategies for enhancing the bioavailability of poorly soluble drugs in nanogels. Colloids Surf B Biointerfaces. 2019;184:110518. doi:10.1016/j.colsurfb.2019.110518.

24. Chhabra G, Thakur D. Applications of nanoparticles in anti-inflammatory therapy. Mater Sci Eng C. 2020;113:111041. doi:10.1016/j.msec.2020.111041.
25. Rahman M, Akter S. Herbal nanogels for topical drug delivery: Formulation and characterization. J Pharm Innov. 2021;16(4):705-716. doi:10.1007/s12247-021-09552-5.
26. Patel M, Bhatt S. Challenges in formulating transdermal systems for pain management. Pharmaceutics. 2020;12(6):563. doi:10.3390/pharmaceutics12060563.
27. Das M, Mohanty C, Sahoo SK. Herbal drugs and nanotechnology: A promising synergy for better therapy. Curr Drug Discov Technol. 2021;18(3):248-265. doi:10.2174/1570163818666200727094501.
28. Sable RR, Thite DG, Udavant PB, Ahire ED, Khairnar SJ. Isolation and identification of flavonoid compounds and formulation of *Tecoma undulata* (Sm.) seem. herbal ointment. *Materials Today: Proceedings.* 2023 Dec 12. doi:10.1016/j.matpr.2023.12.045.
29. Sharma R, Singh V. Anti-inflammatory and analgesic potential of herbal formulations: A comparative study. J Pharm Sci. 2022;111(3):729-739. doi:10.1016/j.xphs.2021.12.025.
30. Sahoo SK, Malhotra M. Advances in drug delivery systems for topical analgesics. J Drug Deliv Sci Technol. 2021;65:102716. doi:10.1016/j.jddst.2021.102716.
31. Ahire E, Thakkar S, Borade Y, Misra M. Nanocrystal based orally disintegrating tablets as a tool to improve dissolution rate of Vortioxetine. *Bulletin of Faculty of Pharmacy, Cairo University*. 2020 Dec 1;58(1&2):11-20. doi:10.21608/bfpc.2020.23944.
32. Bhatia D, Chugh NA. Topical delivery systems for herbal bioactives: Trends and perspectives. Phytomedicine. 2020;76:153235. doi:10.1016/j.phymed.2020.153235.
33. Roy P, Roy R. Nanoparticles-based formulations for skin disorders. Int J Nanomedicine. 2021;16:1153-1175. doi:10.2147/IJN.S299354.
34. Gupta A, Agrawal A. Formulation and evaluation of herbal analgesic nanogels. Indian J Pharm Educ Res. 2020;54(3):626-634. doi:10.5530/ijper.54.3.108.
35. Joshi M, Butola R. Advances in transdermal drug delivery using nanotechnology. Adv Drug Deliv Rev. 2021;177:113952. doi:10.1016/j.addr.2021.113952.
36. Aher P, Surana K, Ahire E, Patil D, Sonawane D, Mahajan S. Development and validation of RP-HPLC method for quantitative determination of 4-amino benzene sulphonamide in sulphonamide hydrochloride. *Trends in Sciences.* 2023 Mar 15;20(6):5209. doi:10.48048/tis.2023.5209.
37. Jain P, Keservani RK, Dahima R. In-vivo characterization of hydrogel for treatment of chemo-radiotherapy induced oral mucositis. *Pharmacology Online*. 2010;1:1016-1025.
38. Chauhan N, Tyagi RK. Synergistic effects of herbal and synthetic drugs in nanogels. J Pharm Biomed Anal. 2022;209:114508. doi:10.1016/j.jpba.2021.114508.
39. Rana P, Kaur G. Pharmacokinetics of herbal formulations in transdermal delivery. Pharm Res. 2020;37(5):84. doi:10.1007/s11095-020-02829-3.
40. Mahmood A, Mandal A. Herbal-based nanogels for transdermal drug delivery: A comprehensive review. Nanomedicine. 2021;16(6):475-491. doi:10.2217/nnm-2021-0023.
41. Banerjee S, Mitra A. Therapeutic potential of nanogels for pain and inflammation management. Eur J Pharm Biopharm. 2020;154:131-146. doi:10.1016/j.ejpb.2020.06.022.
42. Elsaied EH, Dawaba HM, Ibrahim EA, AfounaMI. Investigation of proniosomes gel as a promising carrier for transdermal delivery of Glimepiride. Universal Journal of Pharmaceutical Research 2016; 1(2): 1-10.http://doi.org/10.22270/ujpr.v1i2.R1
43. Anyanwu NCJ, Adogo LY, Ajide B. Development and evaluation of in situ gelling gastroretentive formulations of Meloxicam. Universal Journal of Pharmaceutical Research 2017; 2(3): 10-13.http://doi.org/10.22270/ujpr.v2i3.R3
44. Obanewa OA, Oyeniran OT. Development and estimation of anti-inflammatory activity of topical etoricoxib emulgel by carrageenan induced paw oedema method.Universal Journal of Pharmaceutical Research 2019; 4(3): 22-26.https://doi.org/10.22270/ujpr.v4i3.265

45. Umar S, Onyekachi MK. Development and evaluation of transdermal gel of Lornoxicam. Universal Journal of Pharmaceutical Research 2017; 2(1): 15-18.http://doi.org/10.22270/ujpr.v2i1.R4
46. Paliwal S, Kaur G, Arya KKR. Formulation and characterization of topical nano emulgel of terbinafine. Universal Journal of Pharmaceutical Research 2018; 3(6): 28-34.https://doi.org/10.22270/ujpr.v3i6.223
47. Algin Yapar E, Beskan U, Karavana SY. A recent overview of locally administered topical otic dosage forms.Universal Journal of Pharmaceutical Research 2019; 4(4): 39-42.https://doi.org/10.22270/ujpr.v4i4.299
48. Arirudran B, Priyadharshini P, Rao USM. Estimation of anti-inflammatory activity as well as apoptotic activity of ethanolic extracts of Crocus sativus. Universal Journal of Pharmaceutical Research 2018; 3(6): 6-11.https://doi.org/10.22270/ujpr.v3i6.217