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Review Article

Recent Update on Topical Drug Delivery Systems: Emulgel

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ABSTRACT

Emulgel is an emerging topical drug delivery system that, if more effort is devoted to its formulation and development with more topically active drugs, will prove to be a boon to skin care and cosmetology. Emulgels are both O/W or W/O emulsions which might be gelled with the aid of mixing with a gelling agent. Incorporating the emulgel increases its stability and makes it controlled release system. Due to the lack of excess oil bases and insoluble excipients, it exhibits better drug release compared to other topical drug delivery systems. The presence of the gel phase makes it non-greasy and promotes good affected person cooperation. Those reviews provide knowledge approximately Emulgel such as its properties, benefits, formulations and its current research advances. All elements consisting of the choice of gelling agent, oil agent, emulsifiers affecting the stability and effectiveness of Emulgel are discussed. All rationales are defined in accordance with study conducted via numerous scientists. After an in depth examine, it could be concluded that Emulgels appear to be a better and greater effective drug delivery system compared to other topical drug delivery systems. A complete analysis of the rheological and release properties will offer insight into the capacity use of the Emulgel formulation as a drug delivery System.

Keywords:- Emulsion, Topical Emulgel, gelling agent, Emulsifier, Thixotropic, Cosmetics.**ARTICLE INFO:** Received 2023; Review Complete 2023; Accepted 2023; Available online 15 August 2023**Cite this article as:**Lilhare KT, Borkar SS, Baheti JR, Recent Update On Topical Drug Delivery Systems: Emulgel, Asian Journal of Pharmaceutical Research and Development. 2023; 11(4):133-138. DOI: <http://dx.doi.org/10.22270/ajprd.v11i4.1299>***Address for Correspondence:**

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INTRODUCTION

Human being have been facing various types of diseases since ages which affect their health and nicely-being. Pathways to the treatment of diseases have led to the discovery of various drugs, medicines and delivery systems. To the drug required for various methods of administration are used in the treatment of the disease. The method of administration depends on the type and severity of the disease. Topical route is very beneficial for skin disorders. Local administration of drugs a system can be defined as the direct application of a drug containing formulation to the skin to achieve a topical effect of the medicine [1]. Topical medication the transport system has few advantages such as the avoiding gastrointestinal incompatibility, metabolic degradation associated with oral administration, ability to deliver the drug more selectively to a specific site. [2] In addition, topical applications provide increased bioavailability by avoiding hepatic first-pass metabolism and administration over longer intervals of time [3,4]. In the system, the drug diffuses out of the application system, reaches the site of movement and is

absorbed through the skin [5]. Consequently, increasing the rate of drug release from the dosage form should improve percutaneous absorption [6]. Drug release rates from topical preparations immediately depend on the physicochemical properties of the provider and the drug used [7,8]. For the reason that the mid-1980s, emulgel have won significance in pharmaceutical topical semi-solid dosage forms. In cosmetics, such hydrophilic systems had been acknowledged for a long term. Emulgels are O/W or W/O emulsions which can be gelatinized by means of mix with the gelling agent [9]. O/W emulsions are most beneficial as water-cleanable it is the general cosmetic purposes, while W/O emulsions are extra extensively used for dry pores and skin remedy and emollient applications [9,10-11]. Because Emulgel has properties of both an emulsion and the gel, it acts as a double controlled release system [12]. It is recognized that the any topical preparation lies in its penetrative capacity and refers back to the removal of the oil from the pores and skin. Pores and Skin penetration approaches are simple if the emulsion is thixotropic. To enhance the stability and penetrative capacity, it is miles incorporated into the gel.

Moreover, gels for dermatological use have numerous favorable properties, such as thixotropic, non-greasy and easy spreadable, easy to remove, emollient, non-staining.^[13,14] Type the concentration of the polymer that forms the gel matrix can affect stability and additionally the rate of release of the incorporated drug^[15,16]. Therefore, in relation to topical administration of a poorly water-soluble drug, Emulgels may serve as a better option. Emulsified gel has been proven to be a stable and better vehicle for hydrophobic or poorly water-soluble drugs^[17,18]. Emulgels

are actually used to treat a variety of species skin diseases, such as the ones infected through viruses, micro organisms and fungi species (eczema, Herpes simplex, acne)^[19]. Emulsion-based gel improvement processes need to be adopted for treatment such forms of disorders. Researches on its cream formulations carried out the use of various plant ingredients such as, *P. coliforliaseeds*, *C. tora*. Emulgel are the anti-inflammatory drug is used to relieve muscle and joint ache.^[20,21]

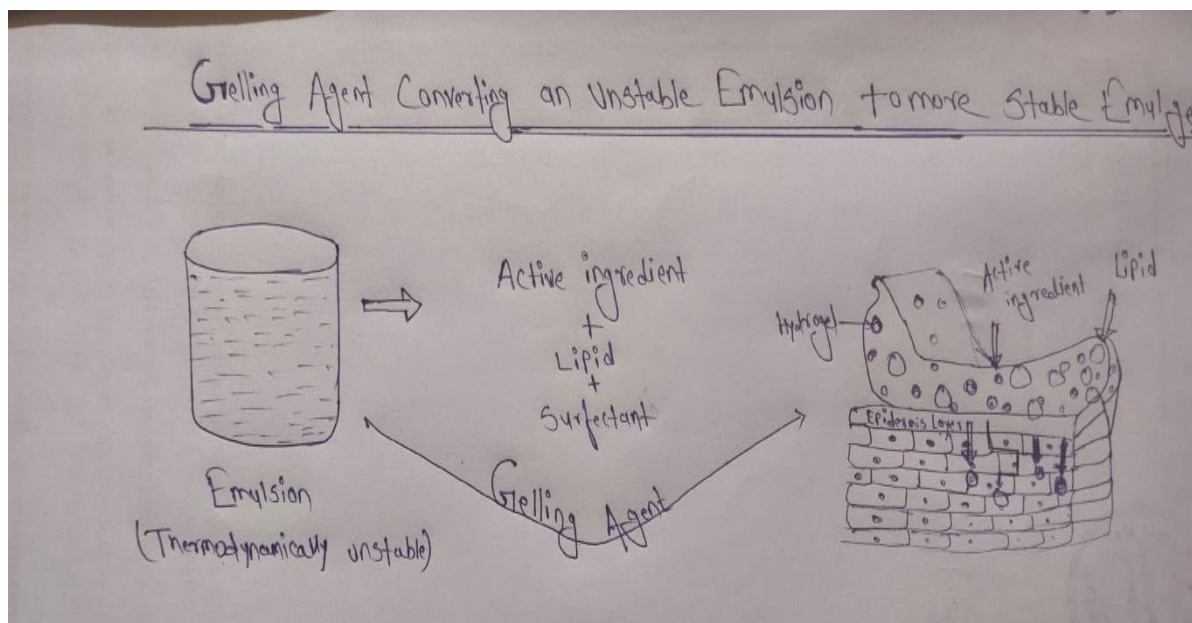


Figure 1: Emulgel penetration through skin.

FORMULATION CONSIDERATIONS

Oil phase selection -

Emulgels are simply emulsions which might be gelled by way of mixing with a gelling agent in order that emulsions can be of the O/W or W/O kind depending on intended use. The material forming the oil phase of the emulsion and their relative amount is primarily determined by the finite product use.^[22] Any formulation must be optimized for the type, meaning and utility of the oil to be used. Investigations of the influence of the oil phase on various parameters such as viscosity, permeability and stability of emulsions have been carried out. Oils extracted from various types of plants have medicinal values, these parts can be used to prepare an effective medicine in the form of the newly developed Emulgel transport system. One such medicinally important oil is Geranium. Geranium is used to stop bleeding, heal wounds, ulcers and skin diseases and to treat diarrhoea, dysentery and colic. The oil has insecticidal and antibacterial properties^[23,24]. Some different medicinal plants have additionally been investigated for their antimicrobial activity, which includes *Arnelia nobilis*, *Vitex nigundu*, *Buniun persicum*, *Acacia concinna*, and *Albizia lebbeck*, *Colla millenii*. Analysis of the ethanolic extracts of the above medicinal plants showed promising antimicrobial agents. potentials against selected test microorganism and fungi^[25]. There someof medicinal plant and their oils can be used in the formula of Emulgel. A number of such oils &

class of drugs for synergistic combination are listed and described in Table 1.

Shahin et al. (2011) carried out one such research work using jojoba oil as the oil phase for Emulgel. They prepared an antifungal Emulgel from clotrimazole the use of jojoba oil as the oil segment. The purpose of selecting jojoba oil because the oil phase was that it could help reduce the inflammation commonly associated with yeast infections. Additionally, it has been found to be effective in fighting inflammation in numerous experimental animal models^[26].

Liquid paraffin and the mineral oil changed into additionally as oil phase of many emulgel formulations.^[27,28-29]

Shrikhande et.al.,2013 carried out one research work using tea tree oil, lemon grass oil, ginger and Capsicum oleoresin and stated that these formulations with cow ghee as an excipient are ideal products with improved pharmacokinetic and pharmacodynamic profiles^[30].

B. Behera et al. (2015) The current look at describes the impact of polyglycerol polyricinoleate (PGPR) on solar radiation properties. Emulgels primarily based on Sun-flower oil and span-40. The effectiveness of metronidazole-saturated emulsifiers as antimicrobial arrangements turned into examined in vitro. *E. coli* was used as a model microorganism for the antimicrobial study. The drug loaded emulgels showed good antimicrobial activity against *E. coli*.

In against, the developed emulgels can be tried for controlled delivery of antimicrobial drugs^[31]

X.-W. Chen et al. (2016) Zein based totally oil-in-glycerol emulgels enriched with b-carotene as margarine alternatives. The have lookat suggests that azein stabilized high (/ = 0.6) oil-in-glycerol (O/G) emulgels enriched with b-carotene become carried out, with aid of facile one step homogenization^[32].

Glicerio Leon Mendez et.al.,(2018) They designed cosmetics based totally on emulgel from crucial oils of thyme, cinnamon and clove and evaluated the pharmacokinetic and pharmacodynamic parameters and ultimately suggested that the emulgel formulation improved both profiles of the chosen drugs and advanced their antioxidant ability^[33].

Mohite et al.(2019) Conducted one such research work using coriandrum sativum seed oil as oil phase for emulgel. stated that the components is optimized and has higher results both in vitro and in vivo and has good anti-inflammatory activity^[34].

P. Nasirpour-Tabrizi et al (2020) carried out one such research work are the Rheological and physicochemical properties of novel low-fat emulgels containing flaxseed oil as a rich source of ω -3 fatty acids.^[35]

M. Rawooh et al. (2020) Carried out one research work on Synthesis and characterization of novel tamarind gum and rice bran oil-based emulgels for the ocular delivery of antibiotics^[36].

Table 1: Different oil Phases are used for emulsion development

Oil	Source	Characteristic	Preparation	Uses
Castor Oil	Ricinus Communis	Vegetable Oil	Microemulsions, Ointment	Antimicrobial
Olive Oil	Olive Seeds	Vegetable Oil	Emulsion, Microemulsion	Anti-Inflammatory Anti-Viral
Birch Oil	Betula Alba	Vegetable Oil	Cream, Ointment, Gel	Analgesic, Antiseptic[43]
Thyme Oil	Thyme Plant	Vegetable Oil	Nanoemulsions, Cream	Anti-Rheumatic[44-47]
Wheat Germ Oil	Wheat Kernel	Vegetable Oil	Microemulsion, Lotion	Anti-Inflammatory
Myrrh Oil	Commiphora Myrrha	Vegetable Oil	Emulsion, Gel	Anti-Microbial Anti-Viral[51]
Flaxseed Oil	Linum Usitatissimum	Vegetable Oil	Emulsion, Gel	Anti-Inflammatory [52]
Tea Tree Oil	Melaleuca Alternifolia	Vegetable Oil	Emulsion, Gel	Anti-Microbial [53]
Lemon Grass Oil	Cymbopogon	Essential Oil	Emulsion, Gel	Anti-Bacterial[53]
Sun-Flower Oil	Helianthus Annuus	Vegetable Oil	Emulsion, Gel	Anti-Inflammatory
Coriander Oil	Coriandrum Sativum	Vegetable Oil	Emulsion, Gel	Anti-Inflammatory [55]
Rice Bran Oil	Oryza Sativa	Vegetable Oil	Emulsion, Gel	Anti-Inflammatory,
Sesame Oil	Sesamum Indicum	Vegetable oil	Emulsion, Gel	Anti-Rheumatic[57]

Selection of Emulsifying agents:-

Emulgels are simply oiled-in-water or water-in-oil emulsions which gel by mixing with a gelling agent such as emulsions. However, the stability of these systems can be significantly increased by using appropriate thermodynamically unstable systems emulsifiers, to reduce interfacial tension, (Fig.3).an emulsifier must have a reasonable balance between its hydrophilic & lipophilic groups to satisfy and be able to produce stable liquid^[58]. Selection of the appropriate concentration is based on experience and trial and error^[59]. Non-ionic surfactants such as spans, tweens have HLB values above 8 and are used in o/w emulsion formulations, whereas mineral oils such as liquid paraffin have HLB values below 8 and are therefore used in water- in -oil emulsion formulations. Emulgel was developed using tween 20 as an emulsifier in tween 20 in its and span 20 in its oil phase^[9,60,61].Both surfactants are sorbitan esters of lauric acid with the same cyclic structure. However, Tween 20 has additional polyoxyethylene units. Tween surfactants are polysorbate molecules, each attached to a hydrophilic head group of oligo (ethylene glycol) (OEG) chains and a hydrophobic fatty acid end.ester group as shown in (Fig. 4)^[71,72,73]. Span 20/Tween 20 blends contribute to greater stability of emulsions in comparison with pure Tween or Span systems^[62].

Selection of Gelling agents

The addition of a gelling agent to these formulations provides a gel structure. Gelling agents are of two types: natural and synthetic. The incorporation of a gelling agent into the system renders it thixotropic^[63]. According to the Swedish National Encyclopedia (1989–1996)^[63], thixotropy is "the property of being viscous (viscid) or gel - like a product that becomes more liquid and more vigorous the longer it lasts, which deforms (e.g. by stirring). It is generally accepted that thixotropy is a fluid phenomenon that exhibits a reversible structure. transition (i.e. gel-sol-gel conversion) due to time dependent changes in viscosity induced by temperature, pH or other components without any changes in the volume of the system (Fig. 5)^[64].The gel-sol-gel imparts stability and also improves bioavailability of the system. However, system stability can be affected by many factors such as pH, temperature, polymer concentration, polymer combinations, additions of cations or anions. Hydroxypropylmethylcellulose is a white to slightly off-white, odorless and tasteless or a granular, free-flowing powder that is a synthetic modification natural polymer cellulose^[65].HPMC based Emulgel is superior to emulgel based Carbopol because it showed a better drug release rate^[9].

Table 02: Different gelling agents used for emulgel formulation

Sr. No.	Gelling agents	Quantity	Dosage form
1.	Carbopol-	1 %	Gel/ Emulgel
2.	Carbopol-	1 %	Gel/ Emulgel
3.	HPMC	3.5%	Gel
4	Sodium	1 %	Gel

Formulation Methods

There are various methods of formulation of Emulgel, employing different kinds of ingredient, one method reported by Rachit Khullar (2011) in his research work (mefenamic acid Emulgel) includes formation of emulsion (o/w or w/o), followed by addition of gelling agent to form Emulgel. Different formulations were prepared using different amounts of gelling agent and penetration enhancers. The method differed only in the process of making the gel in a different formulation. The preparation of the emulsion was the same for all formulations. The gel phase in the formulations was prepared by dispersing Carbopol 940 in purified water with constant stirring at

moderate speed on a mechanical shaker, then the pH was adjusted to 6–6.5 with tri ethanolamine (TEA). The oil phase of the emulsion was prepared by dissolving span 20 in light liquid paraffin, while the aqueous phase was prepared by dissolving tween 20 in purified water. Methyl and propyl parabens were dissolved in propylene glycol, while mefenamic acid was dissolved in ethanol and both solutions were mixed with the aqueous phase. Clove oil and mentha oil were mixed in the oil phase. Both the oil and aqueous phases were heated separately to 70–80 °C, then the oil phase was added to the aqueous phase with constant stirring until it cooled to room temperature. The resulting emulsion was mixed with gel in a ratio of 1:1 with gentle stirring to obtain an emulgel (Jain et al.,2011)^[66].

Routes of administration

Topical administration generally means direct application of the drug to skin to the site of action.

Table 3: Emulgels with different categories of drugs & their routes of administration.

DRUG	AIM	ROUTE	USES
Itraconazole	Improvement of gellified emulsion for controlled drug delivery of itraconazole	Topical	Blastomycosis, histoplasmosis ^[67]
Diclofenac sodium	Evaluation of antimicrobial of prepared Emulgel formulations	Topical	Anti-inflammatory, Analgesic ^[68]
Mefenamic acid	Guidance of Emulgel of mefenamic acid the use of Carbopol as gelling	Topical	Anti-inflammatory ^[69]
Ketorolac trometamol	Systemic drug delivery of ketorolac transdermal route through cast	Topical	Highly analgesic ^[70]

Marketed preparation

Following in Table 4 are the emulgels that are prepared and marketed commercially.

Table 4: Emulgels that are prepared and marketed commercially

Sr. No.	Brand Name	Active Ingredient	Manufacturer	Uses
1.	Avindo Gel	Azithromycin	Cosme pharmaceutical	Anti-inflammatory
2.	Cataflam Emulgel	Diclofenac potassium	Novartis	Anti-inflammatory
3.	Dermafeet Emulgel	Urea 40%	Herbitas Intense	exfoliation activity
4.	Isofenemulgel	Ibuprofen	Beitjalapharmaceuticals	Anti-inflammatory
5.	Miconaz -H- Gel	Miconazole nitrate ,Hydrocortisone	Medical Union pharmaceuticals	Topical corticosteroid & antifungal
6.	Voltarol Emulgel	Diclofenac	Novartis	Anti-inflammatory
7.	Diclomaxemulgel	Diclofenac sodium	Torrent pharma	Anti-inflammatory
8.	Voltaren	Diclofenac diethylamine	Novartis pharma	Anti-inflammatory

CONCLUSIONS

This article reviewed efficiently reviewed about emulgels as it covered all the major points and issues, also highlighted their importance. Some Emulgel arrangements are commercially available in the markets indexed below in Table Isofen Emulgel is a topical analgesic gel that gives comfort again relief of pain. Avindo Emulgel is available in a 30g tube and is a white, pleasant-smelling, non-greasy gel. Isofenemulgel (ibuprofen) anti-inflammatory drug is the active ingredient. It is beneficial for rheumatic conditions. A

similar type available on the market has the trade name Diclomax Emulgel, manufactured by Torrent Pharma.

REFERENCES

1. Zignani M, Tabatabay C, Gurny R. Topical semi-solid drug delivery: kinetics and tolerance of ophthalmic hydrogels. *Advanced drug delivery reviews*. 1995 Aug 1; 16(1):51-60.
2. Kikwai L, Babu RJ, Prado R, Kolot A, Armstrong CA, Ansel JC, Singh M. In vitro and in vivo evaluation of topical formulations of spantide II. *AapsPharmSciTech*. 2005 Dec;6(4):E565-72.
3. Moshfeghi AA, Peyman GA. Micro-and nanoparticulates. *Advanced drug delivery reviews*. 2005 Dec 13; 57(14):2047-52.

4. Rosen H, Abribat T. The rise and rise of drug delivery. *Nature Reviews Drug Discovery*. 2005 May; 4(5):381-5.
5. Zi P, Yang X, Kuang H, Yang Y, Yu L. Effect of HP β CD on solubility and transdermal delivery of capsaicin through rat skin. *International journal of pharmaceutics*. 2008 Jun 24;358(1-2):151-8.
6. Shokri J, Azarmi S, Fasihi Z, Hallaj-Nezhadi S, Nokhodchi A, Javadzadeh Y. Effects of various penetration enhancers on percutaneous absorption of piroxicam from emulgels. *Research in Pharmaceutical Sciences*. 2012 Oct; 7(4):225.
7. Foldvari M. Non-invasive administration of drugs through the skin: challenges in delivery system design. *Pharmaceutical science & technology today*. 2000 Dec 1; 3(12):417-25.
8. Elsayed MM, Abdallah OY, Naggar VF, Khalafallah NM. Lipid vesicles for skin delivery of drugs: reviewing three decades of research. *International journal of pharmaceutics*. 2007 Mar 6; 332(1-2):1-6.
9. Mohamed MI. Optimization of chlorphenesin emulgel formulation. *The AAPS journal*. 2004 Sep;6(3):81-7.
10. Dobrovolskaia MA. Understanding nanoparticle immunotoxicity to develop safe medical devices. The immune response to implanted materials and devices. 2017:63-80.
11. Alexander A, Dwivedi S, Giri TK, Saraf S, Saraf S, Tripathi DK. Approaches for breaking the barriers of drug permeation through transdermal drug delivery. *Journal of Controlled Release*. 2012 Nov 28; 164(1):26-40.
12. Jain, P. Deveda, N. Vyas, J. Chauhan, Development of antifungal emulsion based gel for topical fungal infection, *IJPRD* 2 (2011) 18–25.
13. Panwar A, Upadhyay N, Bairagi M, Gujar S, Darwhekar G, Jain D. Emulgel: a review. *Asian J Pharm Life Sci*. 2011; 2231:4423.
14. Sarisozen C, Vural I, Levchenko T, Hincal AA, Torchilin VP. PEG-PE-based micelles co-loaded with paclitaxel and cyclosporine A or loaded with paclitaxel and targeted by anticancer antibody overcome drug resistance in cancer cells. *Drug Delivery*. 2012 May 1;19(4):169-76.
15. A.A.Kale, V.P. Torchilin, "Smart" drug carriers: PEGylated TATp-modified pH-sensitive liposomes, *J. Liposome Res*. 17 (2007) 197–203.
16. O.E. Philippova, A.R. Khokhlov, 1,13-polymer gels, in: Editors-in-Chief: M. Krzysztow, M. Martin (Eds.) *Polymer Science: A Comprehensive Reference*, Elsevier, Amsterdam, 2012, pp. 339–366.
17. Dickinson E. Hydrocolloids as emulsifiers and emulsion stabilizers. *Food hydrocolloids*. 2009 Aug 1;23(6):1473-82.
18. Ajazuddin, Alexander A, Khan J, Giri TK, Tripathi DK, Saraf S, Saraf S. Advancement in stimuli triggered in situ gelling delivery for local and systemic route. *Expert opinion on drug delivery*. 2012 Dec 1;9(12):1573-92.
19. Raut S, Uplanchiwar V, Bhadoria S, Gahane A, Jain SK, Patil S. Comparative evaluation of zidovudine loaded hydrogels and emulgels. *Res J Pharm Technol*. 2012 Jan 28;5:41.
20. Caddeo C, Sales OD, Valenti D, Sauri AR, Fadda AM, Manconi M. Inhibition of skin inflammation in mice by diclofenac in vesicular carriers: liposomes, ethosomes and PEVs. *International journal of pharmaceutics*. 2013 Feb 25;443(1-2):128-36.
21. Rahmani-Neishaboor E, Jallili R, Hartwell R, Leung V, Carr N, Ghahary A. Topical application of a film-forming emulgel dressing that controls the release of stratifin and acetylsalicylic acid and improves/prevents hypertrophic scarring. *Wound Repair and Regeneration*. 2013 Jan;21(1):55-65.
22. J. Khan, A. Alexander, Ajazuddin, S. Saraf, S. Saraf, Recent advances and future prospects of phyto-phospholipid complexation technique for improving phar-macokinetic profile of plant actives, *J. Control. Release*.
23. Rahmani-Neishaboor E, Jallili R, Hartwell R, Leung V, Carr N, Ghahary A. Topical application of a film-forming emulgel dressing that controls the release of stratifin and acetylsalicylic acid and improves/prevents hypertrophic scarring. *Wound Repair and Regeneration*. 2013 Jan; 21(1):55-65.
24. K. Bowey, J.F. Tanguay, M. Tabrizian, Liposome technology for cardiovascular disease treatment and diagnosis, *Expert Opin. Drug Deliv*. 9 (2012) 249–265.
25. Sawant RR, Torchilin VP. Multifunctionality of lipid-core micelles for drug delivery and tumour targeting. *Molecular membrane biology*. 2010 Oct 1; 27(7):232-46.
26. Habashy RR, Abdel-Naim AB, Khalifa AE, Al-Azizi MM. Anti-inflammatory effects of jojoba liquid wax in experimental models. *Pharmacological research*. 2005 Feb 1; 51(2):95-105.
27. Jain A, Deveda P, Vyas N, Chauhan J, Khambete H, Jain S. Development of antifungal emulsion based gel for topical fungal infection (s). *IJPRD*. 2011; 2(12):18-22.
28. Deveda P, Jain A, Vyas N, Khambete H, Jain S. Gellified emulsion for sustain delivery of itraconazole for topical fungal diseases. *International Journal of Pharmacy and Pharmaceutical Sciences*. 2010; 2(1):104-12.
29. Bhanu PV, Shanmugam V, Lakshmi PK. Antimicrobial preservative activity of the formulated diclofenac emulgel, a novel drug delivery for topical use. *The Pharma Professionals*. 2011;1(1):5-10.
30. Shrikhande PV. Formulation and evaluation of polyherbal topical anti-inflammatory emulgel. *Research journal of pharmacy and technology*. 2013; 6(1):11.
31. Behera B, Biswal D, Uvanesh K, Srivastava AK, Bhattacharya MK, Paramanik K, Pal K. Modulating the properties of sunflower oil based novel emulgels using castor oil fatty acid ester: Prospects for topical antimicrobial drug delivery. *Colloids and Surfaces B: Biointerfaces*. 2015 Apr 1; 128:155-64.
32. Chen XW, Fu SY, Hou JJ, Guo J, Wang JM, Yang XQ. Zein based oil-in-glycerol emulgels enriched with β -carotene as margarine alternatives. *Food chemistry*. 2016 Nov 15;211:836-44.
33. Leon-Méndez G, Osorio-Fortich M, Ortega-Toro R, Pajaro-Castro N, Torrenegra-Alarcón M, Herrera-Barros A. Design of an emulgel-type cosmetic with antioxidant activity using active essential oil microcapsules of thyme (*Thymus vulgaris* L.), Cinnamon (*Cinnamomum verum* J.), and clove (*Eugenia caryophyllata* T.). *International Journal of Polymer Science*. 2018 Jan 1; 2018.
34. Mohite S, Salunkhe A. Formulation and evaluation of Emulgel containing Coriandrum sativum seeds oil for Anti-inflammatory activity. *Journal of Drug Delivery and Therapeutics*. 2019 Jun 15;9(3-s):124-30.
35. Nasirpour-Tabrizi P, Azadmard-Damirchi S, Hesari J, Heshmati MK, Savage GP. Rheological and physicochemical properties of novel low-fat emulgels containing flaxseed oil as a rich source of ω -3 fatty acids. *LWT*. 2020 Nov 1; 133:110107.
36. Rawooh M, Qureshi D, Hoque M, Prasad MG, Mohanty B, Alam MA, Anis A, Sarkar P, Pal K. Synthesis and characterization of novel tamarind gum and rice bran oil-based emulgels for the ocular delivery of antibiotics. *International Journal of Biological Macromolecules*. 2020 Dec 1;164:1608-20.
37. Maissa C, Guillon M, Simmons P, Vehige J. Effect of castor oil emulsion eyedrops on tear film composition and stability. *Contact Lens and Anterior Eye*. 2010 Apr 1;33(2):76-82.
38. Zhu K, Zhou H, Qian H. Antioxidant and free radical-scavenging activities of wheat germ protein hydrolysates (WGPH) prepared with alcalase. *Process Biochemistry*. 2006 Jun 1;41(6):1296-302.
39. Lawrence MJ, Rees GD. Microemulsion-based media as novel drug delivery systems. *Advanced drug delivery reviews*. 2000 Dec 6;45(1):89-121.
40. Di Mattia CD, Sacchetti G, Mastrocola D, Pittia P. Effect of phenolic antioxidants on the dispersion state and chemical stability of olive oil O/W emulsions. *Food research international*. 2009 Oct 1;42(8):1163-70.
41. Lupi FR, Gabriele D, Facciolo D, Baldino N, Seta L, De Cindio B. Effect of organogelator and fat source on rheological properties of olive oil-based organogels. *Food Research International*. 2012 Apr 1;46(1):177-84.
42. Hartman C, Ben-Artzi E, Berkowitz D, Elhasid R, Lajterer N, Postovski S, Hadad S, Shamir R. Olive oil-based intravenous lipid emulsion in pediatric patients undergoing bone marrow transplantation: a short-term prospective controlled trial. *Clinical Nutrition*. 2009 Dec 1;28(6):631-5.
43. Jäger S, Laszczyk MN, Scheffler A. A preliminary pharmacokinetic study of betulin, the main pentacyclic triterpene from extract of outer bark of birch (*Betula alba* cortex). *Molecules*. 2008 Dec 18;13(12):3224-35.
44. Pires C, Ramos C, Teixeira G, Batista I, Mendes R, Nunes L, Marques A. Characterization of biodegradable films prepared with hake proteins and thyme oil. *Journal of Food Engineering*. 2011 Aug 1;105(3):422-8.
45. Ziani K, Chang Y, McLandsborough L, McClements DJ. Influence of surfactant charge on antimicrobial efficacy of surfactant-stabilized thyme oil nanoemulsions. *Journal of agricultural and food chemistry*. 2011 Jun 8;59(11):6247-55.
46. Lee SJ, Umano K, Shibamoto T, Lee KG. Identification of volatile components in basil (*Ocimum basilicum* L.) and thyme leaves (*Thymus vulgaris* L.) and their antioxidant properties. *Food Chemistry*. 2005 Jun 1;91(1):131-7.

47. Fei Lu, Ding Yc, Ye Xq, Ding Yt. Antibacterial effect of cinnamon oil combined with thyme or clove oil. *Agricultural Sciences in China*. 2011 Sep 1;10(9):1482-7.
48. Karabacak M, Kanbur M, Eraslan G, Sarica ZS. The antioxidant effect of wheat germ oil on subchronic coumaphos exposure in mice. *Ecotoxicology and environmental safety*. 2011 Oct 1;74(7):2119-25.
49. Malecka M. Antioxidant properties of the unsaponifiable matter isolated from tomato seeds, oat grains and wheat germ oil. *Food Chemistry*. 2002 Nov 1;79(3):327-30.
50. Jing F, An X, Shen W. The characteristics of hydrolysis of triolein catalyzed by wheat germ lipase in water-in-oil microemulsions. *Journal of Molecular Catalysis B: Enzymatic*. 2003 Oct 1;24:53-60.
51. Tipton DA, Lyle B, Babich H, Dabbous MK. In vitro cytotoxic and anti-inflammatory effects of myrrh oil on human gingival fibroblasts and epithelial cells. *Toxicology in vitro*. 2003 Jun 1;17(3):301-10.
52. Lim WY, Chan EW, Phan CW, Wong CW. Emulsion formulated using *Hibiscus tiliaceus* L. extract and flaxseed oil for topical application. *Industrial Crops and Products*. 2022 Nov 15;188:115718.
53. Shrikhande PV. Formulation and evaluation of polyherbal topical anti-inflammatory emulgel. *Research journal of pharmacy and technology*. 2013;6(1):x
54. Yin WT, Shi R, Li K, Wang AN, Zhao YH, Zhai ZQ. Effect of microwave pretreatment of sunflower kernels on the aroma-active composition, sensory quality, lipid oxidation, tocopherols, heterocyclic amines and polycyclic aromatic hydrocarbons of sunflower oil. *LWT*. 2022 Dec 1;170:114077.
55. Msaada K, Jemia MB, Salem N, Bachrouh O, Sriti J, Tammar S, Bettaieb I, Jabri I, Kefi S, Limam F, Marzouk B. Antioxidant activity of methanolic extracts from three coriander (*Coriandrum sativum* L.) fruit varieties. *Arabian Journal of Chemistry*. 2017 May 1;10:S3176-83.
56. Martillanes S, Rocha-Pimienta J, Gil MV, Ayuso-Yuste MC, Delgado-Adamez J. Antioxidant and antimicrobial evaluation of rice bran (*Oryza sativa* L.) extracts in a mayonnaise-type emulsion. *Food chemistry*. 2020 Mar 5;308:125633.
57. Chopra H, Shrivastav A, Ahmad Y. Formulation and Evaluation of Vegetable Oil Based Emulgel of Fluconazole. *Journal of Drug Delivery and Therapeutics*. 2019 Jul 15;9(4):415-8.
58. Sklenár Z, Horáková K, Bakhouch H, Slanar O. Magistral prepared lidocaine-gel for topical application on skin. *Ceska a Slovenska Farmacie: Casopis Ceske Farmaceuticke Spolecnosti a Slovenske Farmaceuticke Spolecnosti*. 2012 Aug 1;61(4):163-8.
59. Singh B, Khurana L, Bandyopadhyay S, Kapil R, Katore OO. Development of optimized self-nano-emulsifying drug delivery systems (SNEDDS) of carvedilol with enhanced bioavailability potential. *Drug Delivery*. 2011 Nov 1;18(8):599-612.
60. Jain A, Gautam SP, Gupta Y, Khambete H, Jain S. Development and characterization of ketoconazole emulgel for topical drug delivery. *Der Chemica Sinica*. 2010.
61. Khunt DM, Mishra AD, Shah DR. Formulation design & development of piroxicam emulgel. *Int J PharmTech Res*. 2012;4(3):1332-4.
62. Vilasau J, Solans C, Gómez MJ, Dabrio J, Mújika-Garai R, Esquena J. Phase behaviour of a mixed ionic/nonionic surfactant system used to prepare stable oil-in-water paraffin emulsions. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*. 2011 Jul 5;384(1-3):473-81.
63. Singla V, Saini S, Joshi B, Rana AC. Emulgel: A new platform for topical drug delivery. *International Journal of Pharma and Bio Sciences*. 2012;3(1):485-98.
64. Lee CH, Moturi V, Lee Y. Thixotropic property in pharmaceutical formulations. *Journal of controlled release*. 2009 Jun 5;136(2):88-98.
65. J. Mewis, N.J. Wagner, Thixotropy, *Adv. Colloid Interface Sci.* 147–148 (2009) 214–227.
66. S. Priyaprasarth, P. Sriamornsak, Effect of source variation on drug release from HPMC tablets: linear regression modeling for prediction of drug release, *Int. J. Pharm.* 411 (2011) 36–42.
67. Khullar R, Kumar D, Seth N, Saini S. Formulation and evaluation of mefenamic acid emulgel for topical delivery. *Saudi pharmaceutical journal*. 2012 Jan 1;20(1):63-7.
68. Peroli L, Pagano C, Mazzitelli S, Rossi C, Nastruzzi C. Rheological and functional characterization of new anti-inflammatory delivery systems designed for buccal administration. *International journal of pharmaceutics*. 2008 May 22;356(1-2):19-28.
69. Deveda P, Jain A, Vyas N, Khambete H, Jain S. Gellified emulsion for sustain delivery of itraconazole for topical fungal diseases. *International Journal of Pharmacy and Pharmaceutical Sciences*. 2010;2(1):104-12.
70. Bhanu PV, Shanmugam V, Lakshmi PK. Antimicrobial preservative activity of the formulated diclofenac emulgel, a novel drug delivery for topical use. *The Pharma Professionals*. 2011;1(1):5-10.
71. Khullar R, Kumar D, Seth N, Saini S. Formulation and evaluation of mefenamic acid emulgel for topical delivery. *Saudi pharmaceutical journal*. 2012 Jan 1;20(1):63-7.
72. El-Setouhy DA, Ahmed El-Ashmony SM. Ketorolac trometamol topical formulations: release behaviour, physical characterization, skin permeation, efficacy and gastric safety. *Journal of Pharmacy and Pharmacology*. 2010 Jan;62(1):25-34.
73. Kerwin BA. Polysorbates 20 and 80 used in the formulation of protein biotherapeutics: structure and degradation pathways. *Journal of pharmaceutical sciences*. 2008 Aug 1;97(8):2924-35.
74. Shen L, Guo A, Zhu X. Tween surfactants: adsorption, self-organization, and protein resistance. *Surface Science*. 2011 Mar 1;605(5-6):494-9.