China Petroleum Processing and Petrochemical Technology

Catalyst Research Volume 23, Issue 2, August 2023 Pp. 379-388

A REVIEW ON MICROEMULGEL FOR TOPICAL DRUG DELIVERY SYSTEM

[1]Kirti (Research Scholar), [2]Lovely Chaurasia, [3]Anshu

IIMT College of Medical Sciences, IIMT University Meerut.

Email Id: Kirtiposwal007@gmail.com

Abstract

For dermatological activity, topical medication administration is most frequently chosen. There are some downsides to topical dose forms including cream, ointments, gels, etc., including stability issues, stickiness, poor absorption, and permeability. Drug solubility, residence duration, lipophilicity, and permeability are some of its limits. A unique strategy using a Microemulsion based gel is developed to get around this. The topical drug delivery technology known as microemulgel combines the advantages of gel and microemulsion and exhibits a dual release control system. To make the drug particles easily pass through the stratum corneum, the globule size of the emulsion is reduced to less than 200 nm to create the microemulgel. Microemulgel provides a number of benefits in addition to penetration, such as being easily spreadable, grease-free, thyrotrophic, transparent, and biocompatible. Many medications from the antibacterial, antifungal, and non-steroidal anti-inflammatory classes are now being investigated for topical delivery using microemulgel formulation. According to the results of the brief investigation, the microemulgel appears to be a more superior and efficient delivery system when compared to other topical drug delivery systems.

Keywords: Microemulgel, Topical drug delivery system, Lipophilicity, permeability, Antibacterial, Antifungal

Introduction:

Topical drug delivery, which has the advantages of bypassing first-pass metabolism and improving the therapeutic effectiveness of the medicine, is described as the administration of a formulation directly via skin to treat a problem. Topical medications penetrate into the deeper layers of the skin or mucous membranes to cause localized effects where they are applied. It offers flexibility to deliver medications to a targeted spot more successfully. It enables the use of medications with a limited therapeutic window and short biological half-life to prolong the duration of action. The topical medication can be used topically via the ocular, rectal, vaginal, and cutaneous routes to any part of the body. The kind and severity of the ailment determine the administration route. To obtain a medicine's localized effect, a drug delivery system might offer direct application of a formulation to the skin. As they administer medications more specifically to a particular place, topical drug delivery systems have various benefits. To avoid the GI intolerance and metabolic breakdown that come with oral dosing, topical application is used [1-3].

Microemulgel:

The topical drug delivery technology known as microemulgel combines the advantages of gel and microemulsion and exhibits a dual release control system. To make the drug particles easily pass through the stratum corneum, the globule size of the emulsion is reduced to less than 200 nm to create the microemulgel. The process of applying a medication formulation directly to the skin to

Catalyst Research Volume 23, Issue 2, August 2023 Pp. 379-388

treat a problem is known as topical drug delivery, which has the advantages of bypassing first-pass metabolism and enhancing the therapeutic effectiveness of the drug [4].

Topical medications penetrate into the deeper layers of the skin or mucous membranes to cause localized effects where they are applied. It offers flexibility to deliver medications to a targeted spot more successfully. It enables the use of medications with a limited therapeutic window and short biological half-life to prolong the duration of action. The topical medication can be used topically via the ocular, rectal, vaginal, and cutaneous routes to any part of the body. The kind and severity of the ailment determine the administration route. To obtain a medicine's localized effect, a drug delivery system might offer direct application of a formulation to the skin. As they administer medications more specifically to a particular place, topical drug delivery systems have various benefits. To minimize GI intolerance and metabolic degradation brought on by oral dosing, topical application is used. According to the physicochemical characteristics of the carrier and the drug, topical administration also offers enhanced bioavailability and consistent delivery of the drug at longer release rates [5].

Hoar and Schulman developed the idea of a micro-emulsion in the 1940s. A Microemulsion is a mixture of liquids that is optically isotropic and thermodynamically stable. It contains water, oil, and amphiphilic. Many medications can be delivered more effectively and have higher bioavailability thanks to the micro-emulsion. A "micro-emulsion" is a transparent, thermodynamically stable dispersion of two immiscible liquids that contains oil and water and is stabilized by molecules of surfactant through the formation of an interfacial film. A kinetically stable liquid dispersion of an aqueous phase, a lipid phase, and a surfactant is referred to as a micro-emulsion. The size of the dispersed particles ranges from 5 to 200 nm, and there is very little oil/water interfacial surface tension [6].

Because of their small (less than 25%) globule size, micro-emulsions are transparent. The micro-emulsion can be formed without a lot of energy input. A co-surfactant is frequently used in addition to the surfactant, the lipid phase, and the aqueous phase. Below fig. 1, the micro-emulsion structure is described. Depending on their composition, microemulsions can be of three different types:

1. Continuous aqueous phases with a scattered oil phase in an oil in water microemulsion.
2. Bi-continuous micro emulsions, in which the system has inter-dispersed microdomains of lipid and aqueous phase.
3. Water in oil micro emulsions, in which the water phase is dispersed in the continuous oil phase.

When micro-emulsion and gels are combined to create micro-emulgel, they exhibit traits from both. By creating an oil-in-water micro-emulsion and incorporating it into the gel base, micro-emulgel aids in the delivery of hydrophobic medications. They offer a wider surface area for drug absorption, and the lipid part increases bioavailability by enhancing drug penetration. Additionally, the micro-emulsion has improved stability because to the gel foundation. Micro-emulgels offer a firmer level of elegance than micro-emulsions, and they are simple to wash if necessary [7].

Catalyst Research Volume 23, Issue 2, August 2023 Pp. 379-388

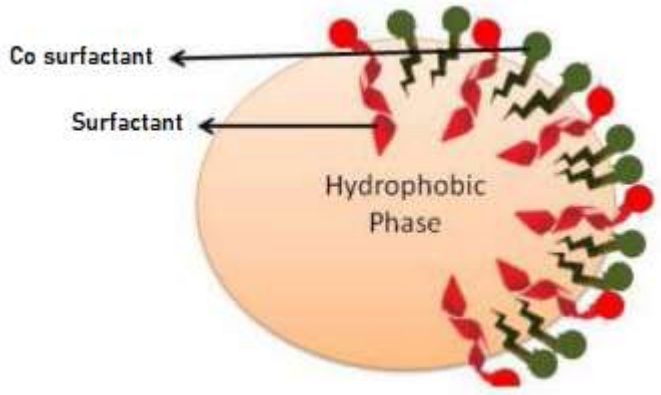


Fig.1: Micro-emulgel Structure

Advantages of Using Micro-Emulgel as a Topical Drug Delivery System:

- With the use of an o/w micro-emulsion, hydrophobic pharmaceuticals can be added to gels with ease.
- Other benefits include better loading capacity, production viability, and cheap preparation costs.
- No intense sonication, controlled release, and the capacity to give medication more precisely to a particular place.
- Preventing gastrointestinal compatibility issues.

Disadvantages of Microemulsion Based Gel:

- The medications with bigger particle sizes are more difficult to absorb through the skin.
- Poor skin permeability for several medications.
- Can only be used for medications whose actions depend on very low plasma concentrations.
- The potential for allergic responses.
- The medications could be denatured by an enzyme in the epidermis.
- Drugs or excipients may cause contact dermatitis, which causes skin irritation [8].

Formulation Considerations:

Selection of Oil Phase:

The carrier oil in which the lipophilic bioactive chemical is dissolved may make up the oil phase [9].

Low molecular weight oils are favoured in the creation of micro-emulsions over high molecular weight oils (such as triglycerides), as they can penetrate the interfacial film and promote the development of an ideal curvature. The inclusion of oil as ripening inhibitors is not necessary because micro-emulsions are thermodynamically stable systems and do not experience instability phenomena like Ostwald ripening [10].

For the purpose of creating a micro-emulsion-based gel, the oil phase that exhibits an excess of drug solubility is chosen. These lipids can have a variety of textures, from mobile liquid to high

Catalyst Research Volume 23, Issue 2, August 2023 Pp. 379-388

solids. There is no need to include a penetration enhancer in the delivery method for micro-emulsions since the lipid phase occasionally serves as a penetration enhancer [11].

The soya-bean oil in a system made up of water, EOs, and Tween-80, according to research. The creation of the system was greatly influenced by soybean oil, which was able to increase the dilatability of EOs-based micro-emulsions and reduced the size of the droplets. Additionally, it helped to lessen the EOs' volatility [12].

Selection of Surfactants:

The ability of selected surfactants to create micro-emulsions with the best possible lipid for medication solubility was supported as the second criterion for surfactant selection [64].

Surfactants are unit-active molecules with a structural structure that includes both a hydrophilic and a lipotropic domain [13].

Surfactants' amphiphilic nature makes it possible for two incompatible phases to disperse while lowering surface tension and creating a sufficiently flexible film that can deform around droplets with the best curvature [14].

They are promptly absorbed by the interface during the emulsification process and prevent the droplets from aggregating [15].

Such systems are stabilized with non-ionic, zwitterionic, cationic, or anionic surfactants. The region of the microemulsion is effective for both ionic and non-ionic surfactants. Polyoxyethylene surfactants like Brij 35, tween-20/80, or sugar esters like sorbitan monooleate (Span 80) are examples of non-ionic embodies [16].

In contrast to micro-emulsions, which are thermodynamically unstable, emulsions are stabilized to some extent by the addition of emulsifying agents by lowering their surface tension. Micro-emulgels are a combination of two dosage forms, such as micro-emulsion and gel. The micro-emulsion is either an oil in water or a water in oil that has been gelled by adding a gelling agent. A good surface-active substance strikes a balance between lipotropic and hydrophilic teams and can create stable emulsions. While mineral oils like liquid paraffin have HLB values less than eight and are used in the formulation of water in oil emulsions, spans and tweens are nonionic surfactants with HLB values more than eight and are used in the formation of o/w emulsions [17].

Selection of Co-surfactants:

Co-surfactants typically consist of short- and medium-chain alcohols as well as polyglycerol derivatives, such as propylene glycol (PG), isopropanol, and isopropyl myristate. Low irritancy co-surfactants have also been produced using nonionic surfactants [18].

To temporarily lower the interfacial tension to a negative value, co-surfactants and surfactant are utilized. Fine droplets are produced by the interface expanding at this negative value, and more surfactant and co-surfactant are adsorbed on the surface until the bulk condition is sufficiently depleted to turn the interfacial tension positive once more. Because the connection between primary surfactant molecules reduces both the polar head group interaction and the hydrocarbon chain interaction, cosurfactant of short-medium chain length alcohols also ensures that the interfacial film is flexible enough to deform easily around droplets [19].

Catalyst Research Volume 23, Issue 2, August 2023 Pp. 379-388

As co-surfactants in micro-emulsion drug delivery systems, polyethylene glycol derivatives of Stearoyl phosphatidyl ethanolamine, ethanol, fatty acid esters of propylene glycol, and oleic esters of polyglycerol, ethyl glycol, and propylene glycol were also investigated [20].

Selection of Gelling Agent:

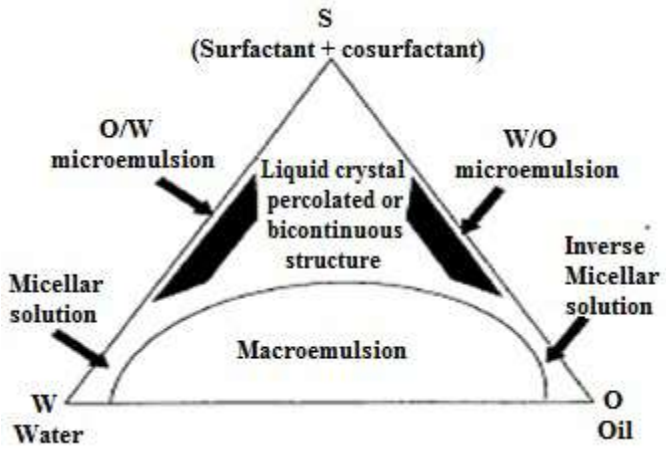
Gel phase is added to formulations to provide the gel structure. Two types of natural and artificial exist. A formulation becomes thixotropic when gel phase is added to it. O/W micro-emulsions and nanoemulsions use thickening agents to balance the density of the oil part with the surrounding liquid part. They may therefore delay the occurrence of the deposit or creaming phenomena by focusing on the impact of the attraction forces [73]. Modifiers for textures are also frequently utilized. In order to prevent the growth of germs, preservative agents must typically be forced into water-based systems. Since EOs are naturally occurring antimicrobials, preservatives are often added on top in the specific situation of EO-based systems. According to the study, EOs-based micro-emulgel was used to successfully encapsulate the antibacterial compound nisin. Through the synergistic effects of nisin and EOs, rosemary, thyme, oregano, and herbaceous plants were selected to increase the system's overall antibacterial activity [21].

According to research, carbopol 980 was utilized as the gel base to create an amphotericin B nano-emulgel that will be an affordable, reliable, and secure carrier for increased and sustained topical delivery [22].

Pseudo-ternary phase diagram:

The water titration method is used to create phase diagrams, define the behavior of mixtures under dilution, and determine the type of structure that occurred in the subsequent emulsification [23].

An oil, water, and surfactant/co-surfactant combination pseudo-ternary phase diagram is created with a set surfactant/co-surfactant weight ratio. By adding materials to the vial and titrating with water, the emulsification region is created. Visual inspection proves that a mono-phasic and biphasic system has formed. After stirring, clean and transparent mixtures can be seen in monophasic systems, while in biphasic systems, turbidity first emerged, then phase separation. just the area where transparent Microemulsion was taken into consideration. Next, the prepared Microemulsion's particle size and poly-dispersity index (PDI) were evaluated [24].



Catalyst Research Volume 23, Issue 2, August 2023 Pp. 379-388

Fig.2 Hypothetical phase regions of microemulsion system of oil (O), water (W), and surfactant + co-surfactant (S) [25].

Formulation Methods of Microemulgel:

Microemulgel may be developed with 3 steps:

Step.1: Preparation of oil in water or water in oil micro-emulsion using oil phase and water phase.

Step.2: Preparation of gel using gelling agent and water by constant stirring and optimization of pH.

Step.3: Incorporation of micro-emulsion into the gel base to formulate microemulgel.

For the preparation of micro-emulsion essentially 2 strategies i.e. low energy and high energy emulsification techniques are used [26-28].

Low Energy Emulsification Technique:

For the creation of the micro-emulsion, low energy techniques outperform high energy methods. The phase inversion technique and the spontaneous approach are both part of the low energy technique. When using the phase inversion technique, oil, water, and a wetting agent are mixed in a precise ratio. The creation of nano-sized drops during a continuous phase is caused by the titration of the oil phase with the aqueous phase as it is constantly stirred. The emulsification process is impacted by the presence of wetting agent and co-surfactant. The type of emulsion that forms depends on the amount of wetting agent employed in the formulation; temperature also affects emulsion formation. They are hydrophilic and of the oil in water type at low temperatures. They are lipophilic and of the water in oil type at higher temperatures. A bi-continuous structure is created when the aqueous phase and oil component micro-emulsify at an intermediate temperature. The spontaneous technique is specifically used for the unstable element; otherwise, the part inversion technique is used to activate a temperature-dependent spontaneous twist of non-ionic material. The emulsions created at partially inversion temperature will reverse while cooling while being continuously stirred. This method is also limited in that it cannot incorporate unstable elements, but the limitation takes into account a lower part inversion temperature by carefully selecting the surfactant [29].

High energy emulsification technique:

By using hard-hitting homogenizers and ultrasonicators, apply strong shear force energy to rupture the interior and inject nano-sized droplets. In this method, the formulation needs external energy to be stabilized [30].

Evaluation of Microemulgel:

Physical Examination:

The physical characteristics of the prepared microemulgel formulations, such as color, texture, phase separation, homogeneity, and pH, are observed [31].

Spreadability Study:

Spreading is necessary for microemulgel to work. The spreadability of the prepared microemulgel is important since it aids in the application of gel to the skin.

To calculate spreadability, a premarket circle of 1 cm in diameter made of gel is placed on a glass plate, on top of which another glass plate is positioned. 500 g of weight may lay on the upper glass

Catalyst Research Volume 23, Issue 2, August 2023 Pp. 379-388

plate for a period of five minutes. The formula below calculates the increase in the diameter spreading:

$$S = M \times L/T$$

M – Weight tied on upper slide;
L – Length of glass slide
T – Time in seconds

Extrudability Study:

It is the capability of micro-emulgel to continuously squeeze out of nozzle from collapsible tube. The crimped end of a closed collapsible tube holding micro-emulgel is firmly pushed, and a clamp is used to prevent any rollback. The micro-emulgel was then extruded out once the tube's cap was separated. The amount of the extruded-out gel is next measured, weighed, and computed.

E= Wt. applied to produced microemulgel on tube (gm)/ area (cm^2)

Drug Content Determination:

When a known quantity of microemulgel is dissolved in an appropriate solvent and thoroughly combined using a sonicator, drug content of the microemulgel can be determined using a spectrophotometer. At a specific wavelength, the absorbance of the sample and the standard are measured [84, 85].

Drug content= Conc. × dilution issue × volume taken × conversion factor

In-vitro diffusion study:

Franz diffusion cell (diffusion area 3.14 cm2 and 15.5 ml cell volume) controls in-vitro drug release. The membrane's surface is evenly coated with microemulgel. Between the donor and consequently the receptor chamber, the membrane is squeezed. The appropriate solvent is poured into the receptor chamber. Once the samples have reached acceptable dilutions, they are collected and subjected to an ultraviolet light spectrophotometer examination to determine their drug content. As a function of time, the total amount of drug release through the membrane is calculated [32].

Microbiological Assay:

The ditch plate method is applied. The preparation and setting of the nutritional agar media are done at room temperature. Using a sterile cotton swab, the bacterial cell suspension is injected onto the medium's surface. Emulsions that have gelled are poured into a deep trench that has been carved out of the plate. The plate is then incubated for 48 hours at 37°C in the anaerobic jar. The diameter of the zone of inhibition is measured.

Stability Studies:

The created micro-emulgel is put through stability tests at the following temperatures for a total of three months: 5, 25, 60, 65, and 75 degrees Celsius. At intervals of 15 days, samples are taken out and evaluated for their physical characteristics, pH, rheological characteristics, drug content, and drug release profiles [33].

Conclusion:

Microemulgel is regarded as the best method for topical distribution since it has several beneficial qualities, including being easily spreadable and removable, being biocompatible, and having a

Catalyst Research Volume 23, Issue 2, August 2023 Pp. 379-388

longer shelf life. By inserting microemulsion into the gel basis, which provides the advantages of both, microemulgel has the capacity to deliver hydrophobic drugs. There are currently very few commercialized microemulgel formulations on the market, but there is a wide area for study and development. In the future, microemulgel will be very useful in skin care.

Reference:

[1] Thakur S, Thakur N and Ghosh SN. Formulation and in-vitro evaluation of Polyherbal Micro-emulgel containing
Tinospora cordifolia and Curcumin for treatment of Arthritis. Int. J. Pharm. Sci. Drug Res., 8, 259-264 (2016).
[2] Udmale RA, Jain NP and Choudhary VM. Microemulgel as a novel approach for enhancing Topical Drug Delivery: A Review. Indo Am. J. P. Sci., 6, 4803-4809 (2019).
[3] Rajput R, Kumar V and Sharma S. Microemulsions: current trends in sustained release drug delivery systems. Int. J. Pharma. Prof. Res., 7, 1326-1332 (2016).

1. Thakur S, Thakur N and Ghosh SN. Formulation and in-vitro evaluation of Polyherbal Micro-emulgel containing
2. Tinospora cordifolia and Curcumin for treatment of Arthritis. Int. J. Pharm. Sci. Drug Res., 8, 259-264 (2016).
3. Udmale RA, Jain NP and Choudhary VM. Microemulgel as a novel approach for enhancing Topical Drug Delivery: A Review. Indo Am. J. P. Sci., 6, 4803-4809 (2019).
4. Rajput R, Kumar V and Sharma S. Microemulsions: current trends in sustained release drug delivery systems. Int. J. Pharma. Prof. Res., 7, 1326-1332 (2016).
5. Mishra A, Panola R, and Rana AC. Microemulsions: as drug delivery system. J Sci Innov Res., 3, 467-474 (2014).
6. Ashara KC, Paun JS, Soniwala MM, Chavda JR, Mendapara VP and Mori NM. Microemulgel: An overwhelming approach to improve therapeutic action of drug moiety. Saudi Pharm. J., 24, 452-457 (2014).
7. Vats S, Saxena C, Easwari TS and Shukla VK. Emulsion based gel technique: novel approach for enhancing topical drug delivery of hydrophobic drugs. Int. J. Pharm. Res., 3, 649-660 (2014).
8. Bachhav YG and Patravale VB. Microemulsion-based vaginal gel of clotrimazole: formulation, in vitro evaluation, and stability studies. Aaps Pharm. Sci. tech., 10, 476-481 (2019).
9. Flanagan J and Singh H. Microemulsions: a potential delivery system for bioactives in food. Critical reviews in food science and nutrition, 46, 221-237 (2016).

10. Wani RR, Patil MP, Dhurjad P, Chaudhari CA and Kshirsagar SJ. Microemulsion based gel: A novel approach in delivery of hydrophobic drugs. Int J Pharm Res Sch., 4, 398-410 (2015).

11. Ma Q, Davidson PM and Zhong Q. Antimicrobial properties of microemulsions formulated with essential oils, soybean oil, and Tween 80. Int J of food microbial., 226, 20-25 (2016).

12. Dhaval M, Devani J, Parmar R, Soniwala MM and Chavda J. Formulation and optimization of microemulsion based sparfloxacin in-situ gel for ocular delivery: in-vitro and ex vivo characterization. J D Sci Tech., 55, 101-373 (2020).

13. Salvia-Trujillo L, Soliva-Fortuny R, Rojas-Graü MA, McClements DJ. and Martín-Belloso O. Edible nanoemulsions as carriers of active ingredients: A review. Annual review food sci. tech., 8, 439-466 (2017).

14. Muzaffar, F, Singh, UK and Chauhan, L. Review on microemulsion as futuristic drug delivery. Int J Pharm Pharm Sci., 5, 39-53 (2013).

15. Kralova, I and Sjöblom, J. Surfactants used in food industry: a review. J D Sci Tech., 30, 1363-1383 (2019).

16. Patel RB, Patel MR, Bhatt KK and Patel BG. Formulation consideration and characterization of microemulsion drug delivery system for transnasal administration of carbamazepine. Bulletin of Faculty of Pharmacy, Cairo University, 51, 243-253 (2013).

17. Kumar, Ajeet, et al. "Irritable Bowel Syndrome with Reference of Alosetron Hydrochloride and Excipient Profile Used in the Manufacturing of Alosetron Tablet-A Review." Journal of Chemical and Pharmaceutical Sciences, vol. 12, no. 03, 2019, pp. 71–78, doi:10.30558/jchps.20191203002.

18. Nastiti CM, Ponto T, Abd E, Grice JE, Benson HA and Roberts MS. Topical nano and microemulsions for skin delivery. Pharm., 9, 37 (2017).

19. Muhammad AS, Daik R and Ramli S. Study on the effect of oil phase and co-surfactant on microemulsion. Malasiyan J Anal Sci., 21, 1406-1416 (2017).

20. Fontana MC, Rezer JFP, Coradini K, Leal DBR and Beck RCR. Improved efficacy in the treatment of contact dermatitis in rats by a dermatological nanomedicine containing clobetasol propionate. Eur j pharm. Biopharm., 79, 241-249 (2011).

21. Kumar, Ajeet, et al. "Irritable Bowel Syndrome with Reference of Alosetron Hydrochloride and Excipient Profile Used in the Manufacturing of Alosetron Tablet-A Review." Journal of Chemical and Pharmaceutical Sciences, vol. 12, no. 03, 2019, pp. 71–78, doi:10.30558/jchps.20191203002.

Catalyst Research Volume 23, Issue 2, August 2023 Pp. 379-388

22. Hussain A, Samad A, Singh SK, Ahsan MN, Haque MW, Faruk A and Ahmed FJ. Nanoemulsion gel-based topical delivery of an antifungal drug: in vitro activity and in vivo evaluation. D D., 23, 642-657 (2016).

23. Bhatt, Pankaj, Vipin Kumar, Richa Goel, et al. "Structural Modifications and Strategies for Native Starch for Applications in Advanced Drug Delivery." BioMed Research International, vol. 2022, 2022, pp. 1–14, doi:10.1155/2022/2188940.

24. Kesavan K, Kant S, Singh PN and Pandit JK. Mucoadhesive chitosan-coated cationic microemulsion of dexamethasone for ocular delivery: in vitro and in vivo evaluation. Current eye research, 38,342-352 (2013).

25. Nandgude T, Patil S, Syed N, Jadhav A and Wani M. Phytoconstituent Based Microemulgel: A Novel Topical Drug Delivery Approach. Int J Res Pharma Sci., 11, 6595-6605 (2020).

26. Bhatt, Pankaj, Ajeet Kumar, and Rahul Shukla. "Nanorobots Recent and Future Advances in Cancer or Dentistry Therapy- A Review." American Journal of PharmTech Research, vol. 9, no. 3, 2019, pp. 321–331, doi:10.46624/ajptr.2019.v9.i3.027.

27. Patel K, Patel R and Patel M. Formulation and characterization of microemulsion based gel of antifungal drug. Pharma Tutor., 2, 79-89 (2014).

28. Lovelyn C and Attama AA. Current state of nanoemulsions in drug delivery. J Bio Nanobiotech, 2, 626 (2011).

29. Al-Snafi, Ali Esmail, et al. "A Review on Prescription and Non-Prescription Appetite Suppressants and Evidence-Based Method to Treat Overweight and Obesity." GSC Biological and Pharmaceutical Sciences, vol. 19, no. 3, 2022, pp. 148–155, doi:10.30574/gscbps.2022.19.3.0231.

30. Chincholkar AM, Nandgude TD and Poddar SS. Formulation of in-situ gelling ophthalmic drops of moxifloxacin. W J Pharma Res., 5, 712–725 (2016).

31. "A Review on Prescription and Non-Prescription Appetite Suppressants and Evidence Based Method to Treat Overweight and Obesity." International Journal of Pharmaceutical Research, vol. 12, no. 01, 2020, doi:10.31838/ijpr/2020.12.01.412.

32. Shah KK, Shiradkar MR and Bindu VH. Transdermal delivery of aceclofenac: Effect of piperine and itsmechanism of action. Int. J. Pharma Bio Sci., 2, 10–18 (2011).

33. Nandgude T, Thube R, Jaiswal N, Deshmukh P, Chatap V and Hire N. Formulation and evaluation of pH induced in-situ nasal gel of salbutamol sulphate. Int J Pharm Sci Nanotechnol., 1, 177–182 (2008).