Review Article

A Critical Review: Preparation and Characterization of Micellar Gel

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Micelles are loosely bound aggregation of several tens or hundreds of atoms, ions or molecules, forming a colloidal particle. Micelles can either passively or actively target their payload to particular tissues in addition to dissolving hydrophobic medicines. Micelles nano-carriers hold the promise of solving the drug solubility issue among the various drug carriers that have been created. Gels are homogenous, semisolid preparations that often include one or more medications in the form of solutions or dispersions in appropriate hydrophilic or hydrophobic base. Now-a-days micellar gel can become promising approach for enhancing drug permeation through skin. Micellar gel shows higher penetration for treating deeply situated infections (example fungal infection). Micellar gel is generally prepared to increase the permeability or penetration of the medication across the skin. Micellar gels mainly used for providing hydrophobic medication which are encapsulated within micelles and deliver it to specific site. These benefits of micellar microparticles open up a lot of potential for the topical distribution of hydrophobic drugs in the future, with increased efficacy and lower production costs. There are several methods used for micelles and gel preparation such as dialysis method, solid dispersion method, microphase separation method, solvent evaporation method, thermal change method, chemical reaction and flocculation method. The characterization for micellar gel is particle size, critical micelles concentration, drug entrapment efficiency, drug content, nuclear magnetic resonance, differential scanning calorimetry, viscosity, spreadability, extrudability, patch test, skin irritation test and *ex vivo* skin permeability test.

Key words: Gel, micellar gel, micelles, polymeric micelles

The hydrophobic property of pharmaceuticals, which is connected to ever-increasing solubility issues for the past 10 y is the main issue facing contemporary pharmaceutical research. At this time, 70 % or more of potential novel drugs are insoluble in organic and aqueous media. Furthermore, 40 % of commercially available oral medicines are regarded as hydrophobic medications. To achieve therapeutic pharmacological effects in the blood, it is required to consider raising the drug dose. Traditionally, nano-sized carriers such as liposomes, niosomes, micelles, emulsions, etc., were used to encapsulate hydrophobic medicines. Even while some of these carriers (like liposome and noisome) have the potential to increase the solubility of hydrophobic drugs, some of them are unable to contain the hydrophobic molecules. Micelles nano-carriers therefore hold the promise of solving the drug solubility issue among the various drug carriers that have been created or are being researcher[1]. However, there is relatively little information available regarding the toxicity of polymeric-micelle carriers, primarily because the toxicity of pharmaceuticals that are not targeted is typically much more severe than that of carriers used in anticancer drug targeting[2]. Block copolymer micelles can either passively or actively target their payload to particular tissues in addition to dissolving hydrophobic medicine[3]. For the solubilization of lipophilic drugs in micelles, which typically have a diameter of 10-100 nm, an

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inner core made up of the hydrophobic sections of the amphiphiles produces an outer space. A palisade or corona made of the hydrophilic building blocks of the amphiphiles encircles the core region. These conformations sterically inhibit the opsonization of blood constituents, preventing macrophage phagocytosis, reducing reticuloendothelial system clearance and prolonging the period of circulation[4]. The structure of micelles is shown in fig. 1. According to the immunoprecipitation, gels are homogenous, semisolid preparations that often include one or more medications in the form of solutions or dispersions in appropriate hydrophilic or hydrophobic bases[5]. Drug gradient in the gel layer is a factor in delivery kinetics. Thus, drug flux is controlled by drug concentration and gel layer thickness. The amount of medication and its solubility in the gel is related[6]. Gels are used to administer a topical medication that has been rubbed onto the skin, the eye or the mucous membrane. Shampoos, colognes, toothpaste, skin and hair care products and other cosmetics[7].

MICELLAR GEL

The polymeric materials promise a variety of future uses, the potential to modify their properties over a wide range has attracted a lot of attention[8]. Over the past few decades, numerous scientists have worked to create strong hydrogels and organogels in an effort to solve this issue[9]. Large concentrations of solvent typically result in gels with poor mechanical characteristics. In various publications, the topical delivery of medications into the deep layers of the skin *via* micelles has been described as a potential means of getting around the limitations of the systems mentioned above. The transport of the therapeutic agent to the target compartment is successfully ensured by topical drug administration *via* micellar system and the possibility of systemic adverse effects is decreased. Drugs that are hydrophobic become more soluble and permeable due to the active medicinal ingredient's micellization. Many dynamic supramolecular structures, including polymeric micelles have been developed in recent years as a result of advances in supramolecular chemistry. Because they have a lower critical micelle concentration than surfactant-derived micelles, Pluronic's, which are block copolymers based on ethylene oxide and propylene oxide can create more stable polymeric micelles. Monomers and micelles coexist above the Critical Micelles Concentration (CMC) in a dynamic equilibrium. A wide range of medications that are difficult to dissolve can be solubilized by polymeric micelles due to their great stability *in vitro* and *in vivo* and strong biocompatibility. There are numerous drug-loaded micelles undergoing various stages of preclinical and clinical testing at the moment. The hydrophobicity of the micelles' core and bridging blocks determines how long the crosslinks (bridges) in physically bonded micellar gels can stay inside the micelles. Rheometrics was used to assess the viscoelastic and gelation kinetics of physically and covalently crosslinked micellar gels. The micellar gel precursor solutions retained a viscous response at low frequencies and an elastic response at high frequencies, according to the results of frequency sweep tests on physically crosslinked micellar gels at temperatures just above the sol-gel transition[10].

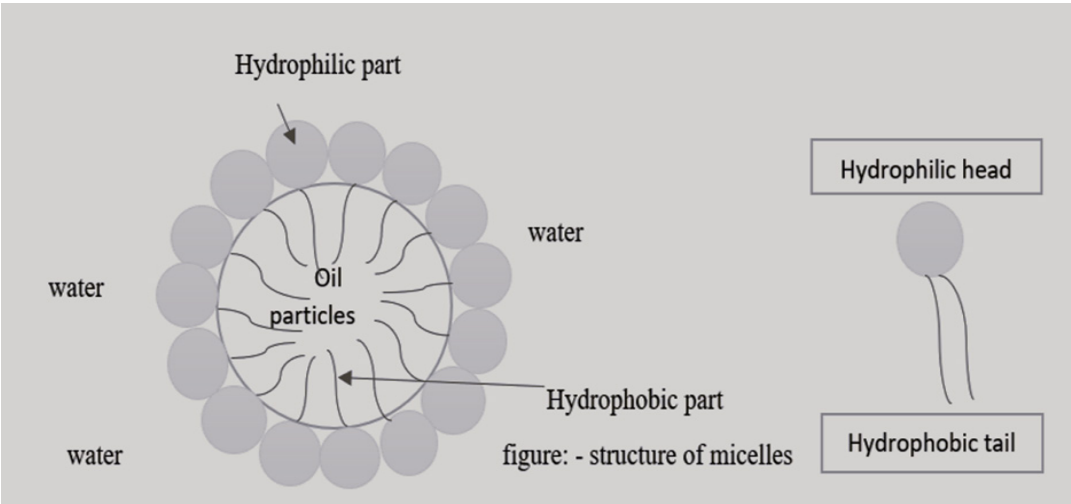

Fig. 1: Structure of micelles

For better foam stability and detergency, viscoelastic worm-like micellar solutions are added to detergents and personal care items like shampoo. Because they have a minimal impact on the environment and gentle on the skin, worm-like micellar compositions employing surfactants from renewable resources are in demand[11]. Rheology allowed us to investigate the mechanical characteristics of the micellar gels produced in the concentrated regime, while light scattering was previously utilised to identify the usual sizes of those micelles in the dilute regime. However, there is currently no information available regarding the micelles' internal structure or how they are organised when they are in the gel state[12].

The first amount of medicine added affects how well a drug is incorporated. Drug precipitates once it has loaded to its maximum capacity. By designing the polymeric core to improve the interaction of the drug with the micelle core, drug release from polymeric micelles can be controlled. There are two main methods that pharmaceuticals are released from the micellar core, either the micelle is dissociated followed by the drug's separation from its monomers or the drug-polymer link breaks within the micelle and is then diffused out of the delivery system[13].

Advantages of micellar gel:

Micellar gels offer several advantages in drug delivery systems. They enable the targeted delivery of medicine to specific sites and allow the encapsulation of hydrophobic medications. Many drugs have high lipophilic character micelles are an effective carrier system for delivering both the hydrophilic and lipophilic drug in tissues. These gels can be produced quickly and cheaply and they have the ability to release molecules gradually over time while circulating in the bloodstream, enhancing penetration capacity compared to other dosage forms[14,15] thereby achieving more penetration capacity than other dosage form. These gels can be produced quickly, cheaply and they have the ability to release molecules gradually over time while circulating in the bloodstream, enhancing penetration capacity compared to other dosage forms. Micellar gels avoid digestive compatibility issues and are convenient and simple to apply offering a larger application area than the buccal cavity, which increases patient compliance. They eliminate the risks and drawbacks associated with intravenous therapy and various absorption-related factors such as pH changes, the presence of enzymes and gastric emptying time. By continuously releasing the medicine, they achieve efficacy with a lower total daily dose and enable precise distribution of medications to particular locations, making them suitable for self-medication.

Disadvantages of micellar gel:

Micellar gels also come with some disadvantages to consider. Firstly, measurement of non-spherical micelles with poor precision and accuracy[16], the influence of temperature, humidity and other environmental factors can change the rheology of some gels[17] and drugs that cause skin irritation or sensitization should not be administered *via* this route[18].

Mechanism of micllelar gel:

Researchers recently revealed a simple approach for making self-healing hydrogels that uses locally produced hydrophilic polymers that have undergone hydrophobic modification along with watchlist management operating in the semi dilute regime. Micellar copolymerization produces dynamic hydrophobic connections between the hydrophobic domains of polymer chains and surfactant micelles, which serve as physical cross-links of the resultant gels. Rapid self-healing of the hydrogels without the requirement for any stimulus or healing agent is achieved by reversible breakable cross-links. The hydrogels gained interest in recent years due to their distinctive properties, such as their insolubility in water but solubility in surfactant solutions, nonergodicity and extreme toughness[19]. However, the mechanism of self-healing and the evolution of the nanoscale structure during the production of micellar hydrogels are still not fully understood. The monomers are transformed into hydrophobically modified hydrophilic polymer chains during micellar polymerization, resulting in a hydrogel with mixed micelles acting as physical cross-links[20].

TOPICAL DRUG DELIVERY SYSTEM

For the purpose of treating local disorders, the term "topical delivery system" refers to a technique in which the formulation is applied to the skin, eyes, nose and vagina. The first pass metabolism of the liver, changes in gastric pH, and fluctuations in plasma levels that are typically experienced when

a drug is delivered orally are avoided when the substance is applied to the topical surfaces. For example, voclosporin (0.2 % w/v) loaded nano micellar formulations were created and their ocular distribution and pharmacokinetics were evaluated by installing single and repeat dosage studies in rabbits. Rapid medication penetration was achieved with just one dose of the topical formulation. Due to their improved drug bioavailability and better capacity to pass through ocular epithelia, micelles are becoming increasingly important in the administration of ocular drugs[21].

METHODS OF FORMULATION OF MICELLAR GEL

The various method of formulation of micellar gel is discussed in fig. 2, which is given below.

Micelles formation:

Dialysis method: The dialysis approach, which used free surfactant was used to create polymeric micelles. Di block copolymers were dissolved in solvent, added to a dialysis tube and dialyzed against 1 l of distilled water over the course of 24 h. The suspension was freeze dried after being filtered using a 0.45 µm filter to remove aggregates (fig. 2)[22].

Oil in water method: Drug was dissolved into chloroform, drug-free polymeric micelles were dissolved into distilled water and homogenised for 30 s using a sonicater. The drug's chloroform solution was stirred vigorously and dropwise into the polymeric micelle solution in distilled water. To remove chloroform by evaporation, the reaction mixture was agitated in an opens air system. After that, the mixture was lyophilized after being ultrafiltered on an Amicon YM-30 membrane to get rid of any remaining unbound drugs and impurities (fig. 3)[23].

Solid dispersion method: This approach involves dissolving the drug and polymer together in an organic solvent, which is then evaporated under decreased pressure to produce a solid polymer matrix. Water is added to the heated polymer matrix to produce drug-loaded polymeric micelles (fig. 4)[24].

Microphase separation method: This technique involves dissolving the medication and the polymer in tetrahydrofuran, an organic solvent and adding the solution dropwise while magnetic stirring is applied to the water. Drugs are included in the inner portion of the polymeric micelles that spontaneously form under lower pressure, the organic solvent is eliminated and a blue-colored polymeric micelles solution is created[25].

Thin film hydration method: In an organic solvent, copolymer, triethylamine and medication solution were dissolved and then combined for 1 h. A drug containing lipid membrane was created by first removing the organic solvent using rotary vacuum evaporation, followed by an additional 30 min of drying under a continuous nitrogen flow. The drug-containing lipid membrane was dissolved in 1 ml of pH 7.4 buffer solution, heated and swirled to create a draught nano micelle solution. After centrifuging this nano micelle solution for 20 min at 13 000 rpm, the final nano micelle was obtained by filtering through 0.22 mm filters (fig. 5)[26].

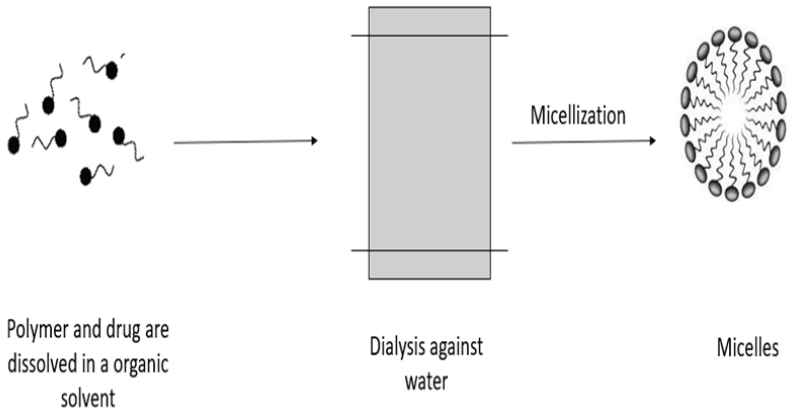

Fig. 2: Network of interactions between the drugs and their targets

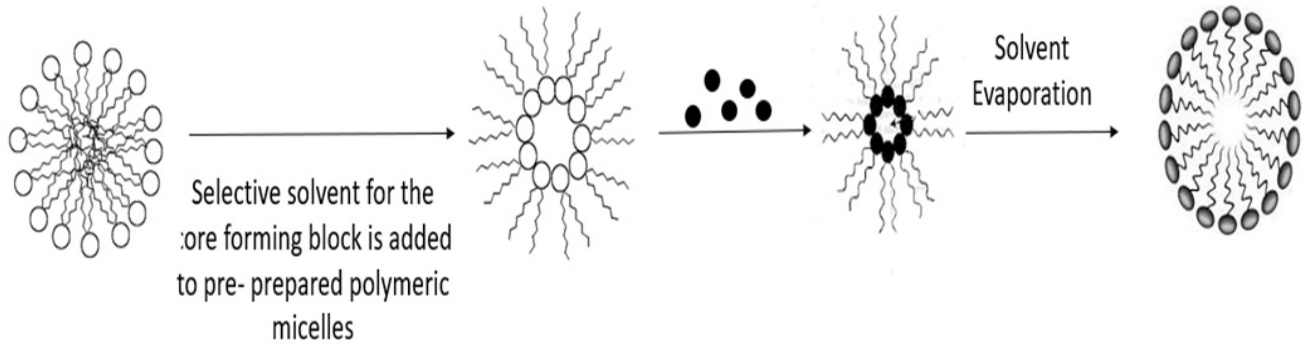

Fig. 3: Oil in water method

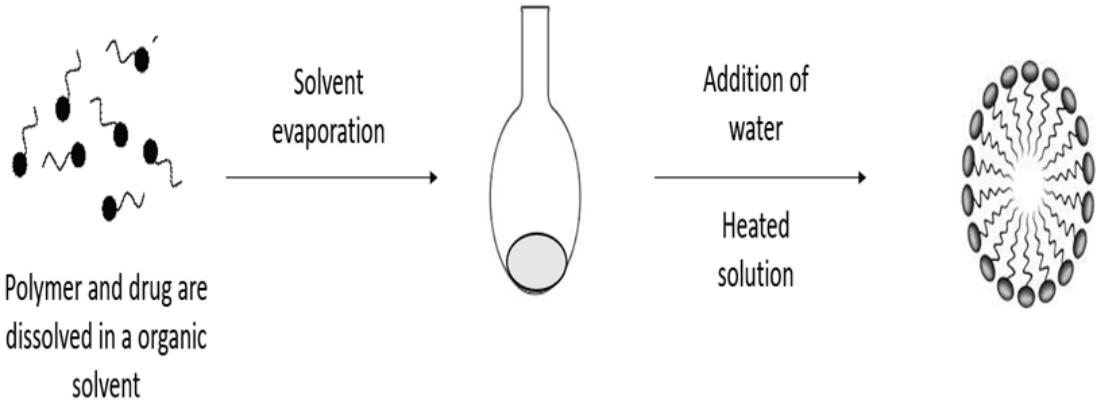

Fig. 4: Solid dispersion method

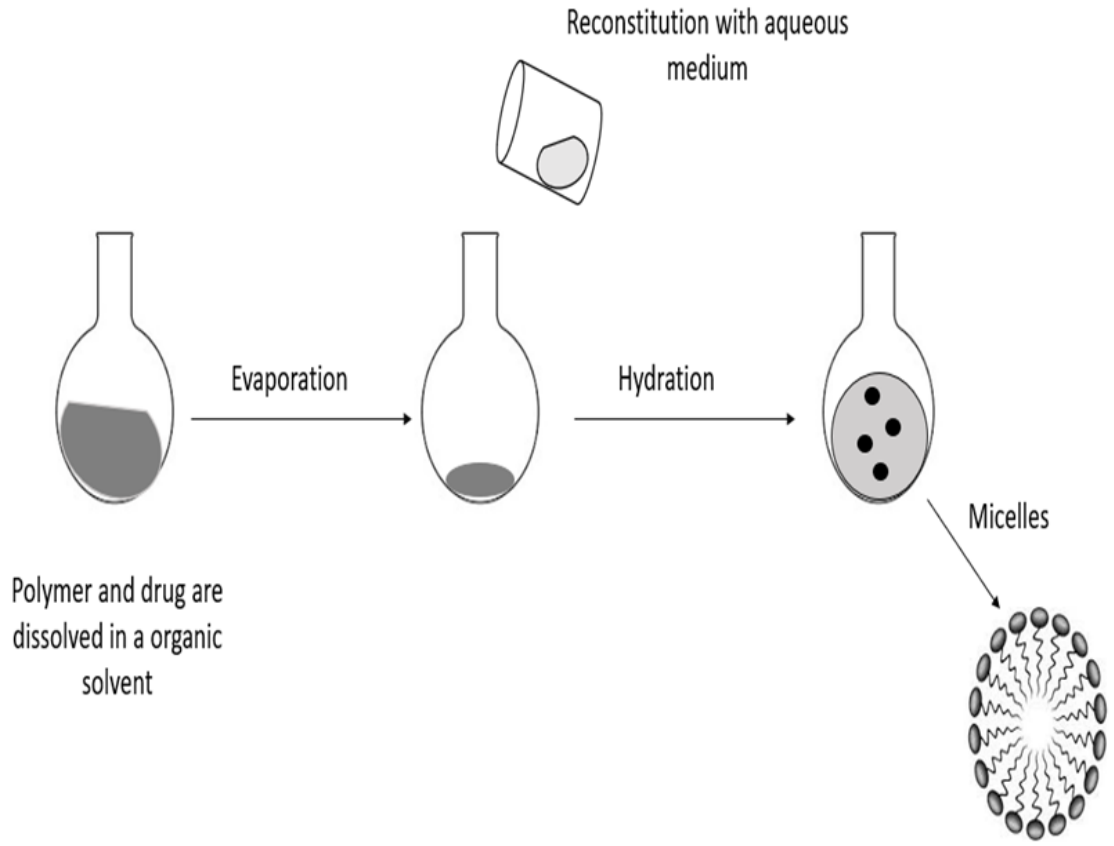

Fig. 5: Thin film hydration method

Solvent evaporation method: Copolymer was typically dissolved in a solvent (ethanol or an ethanol/chloroform combination), which was then vigorously stirred into distilled water to cause the production of micelles. In order to evaporate the solvent and create the "core-shell" blank micelles, the solution was exposed to the air and stirred continuously all night (fig. 6)[27].

Freeze drying: The polymer and medicine are dissolved using the freeze-drying technique using a freeze-dryable organic solvent, such as tert-butanol. Following the addition of water, this solution is freeze dried and reconstituted using isotonic aqueous media. This approach is only applicable to block copolymers and drug structures that can be solubilized in tert-butanol, even if it may be pharmaceutically practical for large-scale manufacture (fig. 7)[28].

Methods of preparation of gel:

The simple method for preparation of gel is discusses in fig. 8, which is given below.

Thermal change method: Cellulose derivatives, gelatin, agar sodium oleate, guar gum, etc. Some substances, such as cellulose ether, on the other hand, have their water solubility due to hydrogen bonding with the water. These solutions lower solubility and broken hydrogen bonds will result in gelation as the temperature is raised. As a result, this technique cannot be used to create gels in general[29].

Flocculation method: Here, gelation is created by adding just the right amount of salt to cause age state precipitation, but not enough to cause full precipitation. In order to prevent a localised high concentration of precipitant, fast mixing must be ensured. For instance, ethyl cellulose and polystyrene solutions in benzene can be quickly mixed with the appropriate proportions of a non-solvent, like petroleum ether. Salts cause coagulation and gelation when added to hydrophobic solutions, respectively. The gels created using the flocculation process behave in a thixotropic way[30].

Chemical reaction method: By a chemical reaction involving the solvent and solute, gel is created in this process. An increased concentration of the reactants will result in a gel structure, as in the case of the formation of aluminium hydroxide gel by interaction of an aluminium salt and sodium carbonate in an aqueous solution. There are a few other cases where the polymeric chain is cross-linked chemically through the reaction of PVA, cyanoacrylates and glycidol ether with toluene diisocyanates, methane diphenyl isocyanine and Tolulene Diisocyanates (TDI)[31].

Complex conservation method:

By combining a polyanion and a polycation, complex coacervate gels can be produced. The fundamental idea behind this procedure is that polymers with opposite charges attract one another and can combine to produce soluble or insoluble complexes, depending on the concentration and pH of the corresponding solutions. For example, combining polycationic chitosan and polyanionic xanthan is one instance of this. Positively charged proteins below their isoelectric point are likely to combine with anionic hydrocolloids to create poly ion complex hydrogels[32].

FACTORS AFFECTING MICELLAR GEL

Thermodynamic and kinetic factors influencing stability:

Polymeric micelles stability can be separated into thermodynamic and kinetic stability, both of which are necessary for *in vivo* drug administration. The polymer chains in micelles are still engaged in a dynamic exchange with those in the medium. To prevent the encapsulated drug cargo from releasing too soon, it is crucial to describe the parameters that affect the stability of micelles. According to reports, the glass transition temperature (Tg) of hydrophobic blocks (or the condition of the micelle core) can significantly affect thermodynamic and kinetic stability, which in turn affects drug release and the pharmacokinetics behaviour of the drug in polymeric micelles.

Critical micelle concentration of polymer:

The tendency for aggregation and thermodynamic stability of Polymer Micelles (PMs) self-assembled by amphiphilic block copolymers with lower CMC are stronger than those of micelles generated by low molecular weight surfactants. Additionally, because the CMC is linked to the standard free energy and the free energy, both of which are useful to the exchange behaviour between micelles and polymer chains, the CMC of polymers may have an impact on the kinetic stability of PMs. Micelles that self-assemble using polymers with lower CMC typically have higher

kinetic stability. The hydrophobic/hydrophilic ratio and interactions between polymers and the environment, such as temperature, pH, and salt concentration parameters, all have an impact on the CMC value.

Ratio of hydrophobicity and hydrophilicity:

The CMC values are mostly influenced by the polymer's hydrophobicity and they decrease as hydrophobicity increases, indicating high stability for PMs. The length of the hydrophobic block can be increased, increasing the polymers' hydrophobicity. The ratio of a copolymer's hydrophilicity to hydrophobicity may alter depending on the length of the hydrophilic block, which may also have an impact on the CMC values.

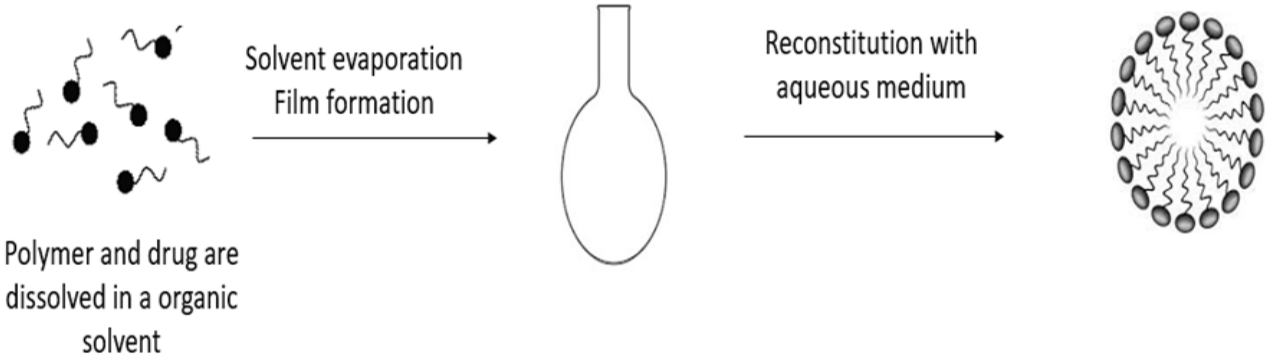

Fig. 6: Solvent evaporation method

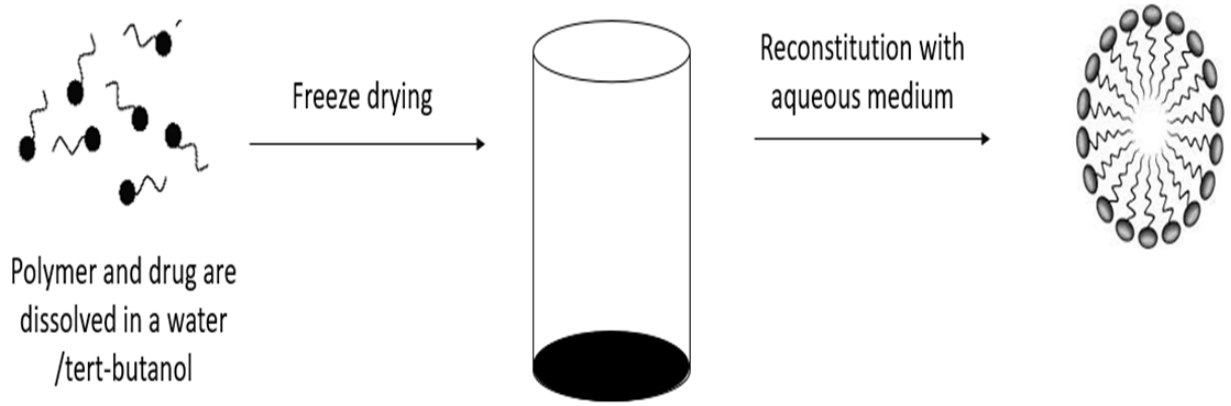

Fig. 7: Freeze drying method

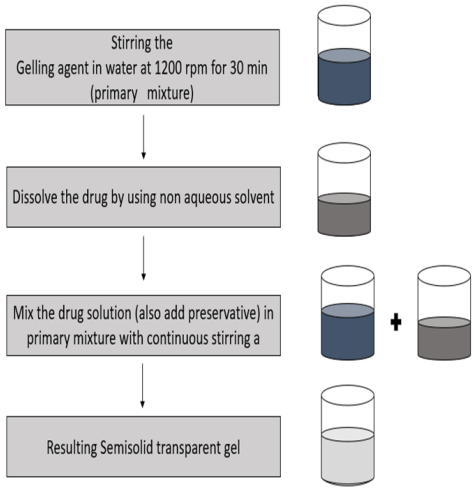

Fig. 8: Methods of preparation of gel

Interaction between polymers: The contacts between polymers, which are essential for the interconversion between micelles and free polymer chains, aid in the production of PMs and preserve their structural stability *in vivo*. These interactions include hydrophobic, electrostatic/ionic, stereo complexation, and hydrogen bonding. As an example, consider hydrogen-bonding compounds where two nucleic acids are enclosed by block copolymers.

Environmental factors: CMC and the size of micelles may be impacted by environmental factors such temperature, salt type or concentration, and pH. The formation of micelles is a temperature-dependent process and even a small rise in temperature may cause a sharp drop in the CMC. The Poly(Ethylene Oxide)-Poly(Propylene Oxide)-Poly(Ethylene Oxide) (PEO-PPO-PEO) block copolymers have been found to produce micelles in water with a strong temperature dependence[33].

Gel microstructure: The three-dimensional gel structure's porosity, which affects how quickly pharmaceuticals diffuse into the environment, is heavily influenced by the amount, size and arrangement of micelles.

MECHANICAL AND RHEOLOGICAL PROPERTIES

The release profile can be maintained by improving these qualities since they can significantly lower gel erosion and drug diffusion rates. For example, poloxamer-based *in situ* gels frequently have extremely porous structures with connected water channels that hasten the erosion of the gel matrix[34].

EVALUATION PARAMETERS OR CHARACTERIZATION OF MICELLAR GEL

Particle size, zeta potential and polydispersibility index:

The size and size distribution of the total amount of drug entrapped in the drug-loaded polymeric micelles were measured after they had been created by film sonication. Laser light scattering was used to determine the composition of the polymeric micelles (Zetasizer Nano ZS, Malvern)[35].

Morphological evolution:

Transmission Electron Microscopy (TEM) was used to observe the morphology of the medication[36].

pH determination:

A digital pH metre was used to measure the pH of micellar gel compositions. After dissolving 1 g of gel in 100 ml of distilled water, it was left to stand for 2 h each formulation's pH was measured three times and using a pH metre, the average results were computed[37].

Grittiness and homogeneity:

All gel preparations must meet the requirements for freedom from specific matter and grittiness as needed for topical applications. Gel formulations were analysed microscopically to look at the particulate debris that was visible under a light microscope. Visual inspection was used to check the homogeneity of all manufactured gels. The appearance and existence of any aggregates in the gels are evaluated[38].

Critical micelle concentration:

By employing pyrene as a fluorescence probe, fluorescence spectroscopy was used to quantify the CMC of the mixed micelles. Pyrene would travel inside micelles from the aqueous phase upon micelle formation, changing the intensity ratio of I372/I383. At room temperature, F-2500 fluorescence spectrophotometer was used to record the fluorescence spectrum. By dilution drug mixed copolymer in distilled water, solutions of various concentrations of drug mixed copolymers were created. Pyrene and the mixed copolymer solution were combined and then the mixture was left to equilibrate for 24 h at room temperature[39].

Determination of drug content in micelles:

Drug-loaded micelles were suitably dissolved in acetonitrile and vortexed to produce a clear solution and then the concentration of the drug was determined using High Performance Liquid Chromatography (HPLC).

Percentage drug concentration=weight of the drug within micelles/weight of the feeding polymer and drug×100 %[39].

Differential Scanning Colorimetry (DSC):

DSC is used to assess the nature and speciation of the crystallinity within micelles. DSC is used to determine the different states of PMs' cores as well as the degree of interactions between drugs and polymers DSC experiments were carried out

to verify that the medication was indeed trapped inside the micelles[40].

HPLC analysis:

The drug's concentration was determined using HPLC. A 0.22 ml membrane filter was used to filter the mobile phase before it was produced and eluted at a rate of 1 ml/min. The drug concentration was calculated using injection volume at 70° and a UV detector set at 210 nm[41].

Entrapment efficacy:

A test tube containing the drug formulation was filled with 10 ml of Phosphate-Buffered Saline (PBS) (pH 7.4). This liquid was subjected to a 10 min sonication in a sonicater bath. Centrifugation was used to separate the drug-containing solution from the unentrapped drug for 30 min at 20° at 25 000 rpm. After being taken out, the supernatant was diluted with PBS. The UV spectroscopic approach was used to measure the drug concentration in the resultant solution. The following equation was used to determine the percentage of medication encapsulation,

EP (%)=[(Ct-Cr)/Ct]×100.

Where, EP is the Encapsulation Percentage, Ct is the concentration of entire drug and Cr is the concentration of free drug[42].

Viscosity:

Micellar gel's viscosity was measured using a Brookfield viscometer[43].

Spreadability:

Using spreadability apparatus, the spreadability of micellar gel formulations was evaluated. A lower slide was used to hold 1.0 g of the micellar gel sample and upper slide as used to cover it. The formula was used to calculate the spreadability[44].

Skin irritation test:

Animal skin, specifically either gender of guinea pig (400-500 g), was used for the skin irritancy test for micellar gel. The hair on the animal's back was trimmed before the micellar gel was applied to a 4 cm^2 of the surface. The guinea pig's skin was exposed to the micellar gel twice daily for 7 d. The site was examined for sensitivity and reaction and it was graded as 0, 1, 2, or 3 for no reaction, light patchy erythema, light but confluent erythema, moderate but patchy erythema and severe erythema without or with edema respectively[45].

Physical stability:

Samples of the formulations were obtained at 1, 7, 14 and 90 d following 3 m of storage at 4°. HPLC-fluorescence was used to evaluate the amount of drug in the formulations of micelles in order to determine how much of it is present[46].

Extrudability test:

Standard collapsible aluminium tubes with caps were filled with the micellar gel compositions and the ends were crimped shut to seal. The tubes weights were recorded. The tubes were placed between two glass slides and then clamped. The cap was removed after 500 g of material had been applied to the slides. We measured the volume of the extruded micellar gel. Calculated extrudability percentages are as follows; >90 % extrudability=excellent, >80 % extrudability=good and >70 % extrudability=fair[47].

***In vitro* drug release:**

The dialysis approach was used in a dialysis bag, 1 ml of polymeric micelles containing drug was placed. Then, a release chamber holding 500 ml of pH 7.4 PBS was filled with the firmly packed dialysis bag. The experiment was carried out at 37° with 100 rpm magnetic stirring that was ongoing. 1 ml of the sample was taken out and immediately replaced with an equal volume of fresh release medium at predetermined intervals. The amount of drug in the sample was determined using HPLC. For comparison, a release study of the medication solution was also carried out[48].

***Ex vivo* skin permeability test:**

A transdermal membrane made of guinea pig abdominal skin was used in *ex vivo* skin permeability testing utilising Franz diffusion cells. Hair on the guinea pigs' abdomens was trimmed with an electric razor. The guinea pigs were gently narcotized with diethyl ether and then a 1.5 cm diameter circular area of abdominal skin was removed using a corneal trephine. The wounds were then sutured and sterilised. The donor chamber was placed between the receiver chamber, which held 5 ml of PBS and the abdomen skin. The donor chamber was in front of the stratum corneum. In the receptor chamber, the PBS was stirred by a magnetic bead (300 rpm). The

diffusion cells were kept at a temperature of 37°. By using HPLC, the medication concentrations in PBS solutions were examined. Plots depicting the cumulative drug concentrations per unit area in the receiver chamber as a function of time were made. The slope of linear part of the line was used to determine the steady-state flux[49].

Statistical analysis:

Data are shown as the mean and standard deviation. The release study's results were statistically analysed using student's t-test[50].

MARKETED PREPARATION OF MICELLAR GELS

Recently many researchers have worked on micellar gel for various diseases like fungal, gynaecological, ocular diseases, psoriasis. But micellar gel has not yet come in the market for medicated purposes. Table 1, provides information on marketed preparations of micellar gel, while Table 2, presents details on research work conducted in various areas involving micellar gel[51-77].

TABLE 1: MARKETED FORMULATIONS OF MICELLAR GEL

S. no	Marketed brand name	Uses
1	Micellair skin breathe (NIVEA)	Make up remover wash gel
2	ACO (sensitive micellar gel)	Cleansing face and eye
3	Micellar gel wash (Dr. Vanitha rattan)	Controlling sebum and skin colour
4	Aveeno (positively radiant)	Draw out skin dulling impurities
5	Babe micellar gel	Cleansing or soothing activity for all type skin
6	Simple water boosts micellar facial gel wash	For removing dirt and make up Instantly restore hydration to dehydrated skin
7	Bioderma sensibio gentle soothing micellar foaming gel	Used for cleansing sensitive skin face and eye

TABLE 2: RESEACH WORK DONE ON MICELLAR GEL IN VARIOUS AREAS

S. no	Drug	Uses	Outcome	References
1	Docetaxel	Breast cancer and ovarian cancer	Formulation having good stabilizing property and also increased the anti-tumour activity	[51]
2	Terbinafine hydrochloride	Onychomycosis	This micellar gel deeper areas of hooves for dermatophytes	[52]
3	Resveratrol	Psoriasis	This formulation treating Plaque psoriasis with superior dermatological outcomes	[53]
4	Paclitaxel	Cutaneous malignancy	local chemotherapy is possible of PTX-micellar gel and inhibited the growth of the melanoma *in vivo*	[54]
5	Curcumin	Eye diseases	These results demonstrated the biocompatible and excellent potential for effective ophthalmic drug therapy	[55]
6	Ibuprofen (IBU) and IBU sodium salt	Analgesic, anti-inflammatory	This formulation increases the therapeutic efficacy through the simultaneous delivery of these agents to a target tissue or organ	[56]
7	Simvastatin	Wound healing	This micellar gel having a good wound healing activity	[57]
8	Curcumin	Ocular diseases	Formulation shows increased the solubility, stability, corneal permeability and no irritant effects on the ocular tissues	[58]
9	Naproxen and indomethacin	Anti-inflammatory	It shows stronger effects partitioning and good drug-water hydrophobic interactions	[59]
10	Paclitaxel (PTX)	Anticancer	The formulation shows good stability and solubility	[60]

11	Miconazole nitrate	Deep fungal diseases	This formulation shows greater permeability and it is more effective at treating ingrained infections	[61]
12	Lurasidone hydrochloride	Bipolar disorders and schizophrenia treatments	It shows prolonged release with improved permeability and brain bioavailability	[62]
13	Griseofulvin and fluconazole	Fungal diseases	It improves the bioavailability and preventing negative side effects than oral dosage form	[63]
14	Doxorubicin and hydrochloride	Anticancer	This micellar gel improving permeability and patient compliance by avoiding repeated drug administration	[64]
15	Ciprofloxacin and hydrochloride	Ocular diseases	This formulation shows prolonged precorneal drug release, improved ocular bioavailability, required fewer administrations, and hence increased patient compliance	[65]
16	Azelastine HCL	Ocular diseases	Successfully deliver a hydrophobic medication in to the eye's anterior portion and cure allergic conjunctivitis	[66]
17	Sirolimus (SIR)	Cutaneous manifestation	It shows good stability	[67]
18	Methoxy poly (ethylene glycol)-polylactide copolymer	Metastasis breast cancers	This formulation shown tumour specific retaining and potent anti-cancer effectiveness against mouse breast cancer	[68]
19	Naproxen	Anti -inflammatory	The formulation shows good permeability across the skin	[69]
20	Clindamycin and isotretinoin	Acne vulgaris	The developed formulation is extremely effective against acne	[70]
21	Itraconazole	Fungal and keratitis	The created formulation shows long-lasting action without irritation, good permeability, and corneal toxicity	[71]
22	Tranylcypromine	Depression	Studies on drug penetration show that the medication's effect was extended release	[72]
23	Ceftiour	To treat deep infections in the bovine foot	Ceftiofur's rate of release was slowed down by a drop in the release medium's temperature	[73]
24	Timolol maleate	For increases ocular bioavailability	According to an *in vivo* study, 0.5 % timolol maleate gel increases the ocular bioavailability in albino rabbits.	[74]
25	Rapamycin	To improve skin permeation of poorly soluble drug	It increasing rapamycin's bioavailability and permeability	[75]
26	Posaconazole	Fungal ocular infections	This micellar gel is a potentially effective drug delivery improve drug ocular penetration and bioavailability	[76]

FUTURE PERSPECTIVES

According to recent research work, micellar gel is used for topical application to cure the various skin diseases or ocular diseases. This dosage form is non-invasive in nature, avoiding first pass metabolism. The limited solubility of hydrophobic drugs makes it difficult for researchers to deliver them to the targeted site. The hydrophobic medication that needs to be applied topically is the main focus here. Micelles help the medication quickly disintegrate at the intended location. Drug administration to a specific place enables sustained drug release while micellar microparticles enhance the solubility and dissolution of poorly soluble medications. These benefits of micellar microparticles open up a lot of potential for the topical distribution of hydrophobic drugs in the future, with increased efficacy and lower production costs. Micellar gel is potentially effective drug delivery to improve drug penetration and bioavailability. The present study of micellar gel with different types of drugs

includes the various uses like breast cancer and ovarian cancer, onychomycosis, psoriasis, deep fungal infections, anti-inflammatory, anticancer, acne vulgaris, etc.

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