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Recent Advances in Novel Drug Delivery System Through Gels: Review

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ABSTRACT

The term gel are semi-solid, three dimensional, polymeric matrices comprising small amounts of solid dispersed in relatively large amount of liquid, yet possessing more solid like character. These systems form a three-dimensional, polymeric matrix in which a high degree of physical reticulation has been comprised. They are formed of long, disordered chains that are connected at specific points, but the connections must be reversible. They are coherent colloid disperse systems at least two components. They exhibit mechanical properties characteristic of the solid state, both the dispersed component and the dispersion medium extend themselves continuously throughout the whole system. Gels are transparent or translucent semisolid formulations containing a high ratio of solvent/gelling agent. When dispersed in an appropriate solvent, gelling agents merge or entangle to form a three-dimensional colloidal network structure, which limits fluid flow by entrapment and immobilization of the solvent molecules. The network structure is also responsible for gel resistance to deformation and hence, its viscoelastic properties. Topical gel formulation provides a suitable delivery system for drugs because they are less greasy and can be easily removed from the skin. Gel formulation provide better application property and stability in comparison to cream and ointments. In this study example, method and structure of gel are discussed to improve the permeability and bioavailability of gels that can be incorporate in to a novel drug delivery system like solid dispersion into gel, emulgel, hydrogel, *in situ* gel, solid lipid nanoparticles into gel and microemulsion gel.

Key words: Gel, skin, solid dispersion, hydrogel, emulgel, microemulsion

INTRODUCTION

Topical dosage forms whether solutions, ointments and cream are intended for administration into eye, rectum, vagina or skin. Skin being the largest organ, in terms of area and easily accessible, it is used as the common site of administration for appropriate topical dosage forms (Gennaro, 2000). The major inherent problem with their delivery system is that regular or systemic absorption of drug through skin is different to be assured (Bachhav and Patravale, 2009; Bhaskar *et al*., 2009; Gaddam and Aukunuru, 2010). The mechanism of drug transportation across the skin is primarily and concentration dependent is a diffusion process. The concentration of the drug at the time can be calculated by using the solubility characteristics of the drug; thus justifying the diffusion (Jain and Pathak, 2010). The topical administration is to be absorbed by the drug molecule to be pass through the biological membrane is a limiting factor of lipid solubility and

molecular size (Ajazuddinm, 2010). Usually the gels are non-greasy and easily washable. These properties have made it be the most popular and acceptable (Suhonen *et al.*, 1999; Velissaratou and Papaioannou, 1989). Gels have gained more and more importance because the gel bases formulation are better percutaneous absorbed than cream and ointment, The formulated gel were evaluated for various physicochemical parameters like pH ,viscosity, spreadability, stability, skin irritation, *in vitro* release and antifungal activity (Babar *et al.*, 1991). The topically used gel have several characteristics like sol-gel transition, non greasy, easily washable, stable and inert (Klich, 1992; Patel *et al.*, 2011). Permeability coefficient of the drug is higher in case of gel due to its higher lipid solubility (Aly and Naddaf, 2006). Other formulation do not provide long term stability, therefore delivery of drug through gels are the better option to overcome the stability of formulation.

A gel is a semi-solid mass of hydrophilic carrier in which all the dispersion medium has been absorbed by the carrier (Atkins, 1990). A gel is a cross linked polymer network and swells in aqueous medium. Gel being composed of two interpenetrating phases (Tanaka, 1987). Hermans gave the definition of gels (Hermans, 1949). The term gels are the suspension of colloidal clays which dispersed at two components, they exhibit mechanical properties characteristic of the solid state and both the dispersed component and the dispersion medium extend throughout the whole system. Gels are defined in USP as semisolid are either suspension of small nonpolar particles or large polar molecules interpenetrated with aqueous (Honrao and Pabari, 2004). Gels are either translucent or transparent semisolid formulations which containing the solubilized ingredient. The gels are constrained within a three-dimensional polymeric matrix (consisting of natural or synthetic gums) in which a high degree of physical cross-linking has been introduced. The matrix structure is responsible for thixotropic behavior. Gels are prepared by either a fusion process or a special procedure used by the gelling agent (Tripathi *et al.*, 1994; Justin-Temu *et al.*, 2004; Kumar and Verma, 2010). In the development of plant tissue culture the gel systems used successively sustained the cultures and found to be cheap and easily available (Daud *et al.*, 2011). The structure of gel colonies and silica gel are given in Fig. 1. Gels are semi-rigid system in which the movement of the dispersing medium is restricted by an interlacing three dimensional network of particles or solvated macromolecules in the dispersed phase (Justin-Temu *et al.*, 2004).

Physical or chemical cross linking may be involved. The interlacing and internal friction is responsible for increased viscosity and their viscosity depends on their polymeric composition. (Lachman *et al.*, 2001; Goodsell, 2004; Neves and Bahia, 2006). Since long creams, ointments, gels and pastes are being used as topical semi solid dosage forms. For the ease of application and

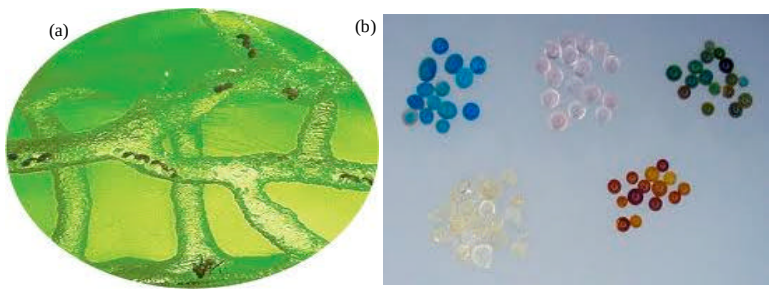

Fig. 1(a-b): Structure of gel (a) Colonies and (b) Silica gel

Table 1: Example of topical gel

Active ingredient	Gelling agent	Route	Use
Acetic acid	Tragacanth, acacia	Vaginal	Restoration and maintenance of acidity
Becaplermin	Sodium CMC	Dermatologic	Promotes healing of diabetic ulcers of lower extremity
Benzoyl peroxide	Carbomer 940	Dermatologic	Acne vulgaris
Clindamycin	Carbomer 934P	Dermatologic	Acne vulgaris
Clobetasol propionate	Carbomer 934P	Dermatologic	Antipruritic
Cyanocobalamin	Methylcellulose	Nasal	Hematologic
Desoximetasone	Carbomer 940	Dermatologic	Anti-inflammatory, antipruritic
Metronidazole	Carbomer 934P	Vaginal	Bacterial vaginosis
Podofilox	Hydroxypropyl cellulose	Rectal	Anogenital warts
Timolol maleate	Gellan gum	Ophthalmic	Treatment of elevated intraocular pressure
Progesterone	Carbomer 934P	Vaginal	Bioadhesive gel for progesterone supplementation and replacement
Tretinoin	Hydroxypropyl cellulose	Dermatologic	Acne vulgaris

important percutaneous absorption gels have been popularity (Wanwimolruk, 1991). Among these the rate and extent of drug release from base determines the therapeutic efficacy of the formulation (Loganathan *et al*., 2001; Najmuddin *et al*., 2010; Snah *et al*., 1991; Patel *et al*., 2011).

Usually the gels are applied to the skin or certain mucous membrane for their local therapeutic effect, emollient or protective effect and sometimes for percutaneous penetration of the drug (Narin, 1997). Gels are commonly prepared by mixing a liquid with suitable thickening agents. The dissolved or dispersed molecules diffuse from the liquid phase through the gel matrix (polymer scaffold) and thus if released in a pattern similar to a solution (Anonymous, 1993; Shivhare *et al*., 2009). Gel formulations are shelf stable and therefore can be used subsequently for the evaluation while storage under different temperatures (Gupta *et al*., 2007; Gupta and Vyas, 2010). In gel the permeation enhancer is used as DMSO (Martis *et al*., 2011). Substances that facilitate the permeation through mucosa are referred to as permeation enhancers (Alexander *et al*., 2011).

Some of the synonyms used to designate the gels are e.g., weak gel, quasi gel, temporary gel, pseudo gel, hetero gel, isogel, microgel and nanogel (Almdal *et al*., 1993; Clark and Ross-Murphy, 1987; Burchard and Ross-Murphy, 1990; Ross-Murphy, 1991; Hermans, 1949; Eicke *et al*., 1990). Some examples of topical gel described in Table 1 and other examples of gels formed by cooling of solutions of biological systems are gelatin Pectin, agarose, carrageenan and agar gels (Almdal *et al*., 1993; Clark and Ross-Murphy, 1987; Russo, 1987; Burchard and Ross-Murphy, 1990). Gelatin is used as natural polymer; it shows excellent property like low cost and low immunogenicity (Wilaiwan *et al*., 2010). Agar is also used as gelling agents and it is most expensive components used in plant tissue culture media (Jain-Raina and Babbar, 2011). Fibrin clots are also typical biological gels which however, are formed by polymerization of fibrinogen monomer through a series of enzymatic reactions (Ferry, 1988). Typical examples of gel, the material used for soft contact lenses like a styrene-divinylbenzene copolymer swollen in an organic solvent and a 2-hydroxyethyl methacrylate ethylene glycol dimethacrylate copolymer swollen in water (Staudinger and Husemann, 1935; Wichterle and Lim, 1960; Refojo, 1979). Silica gel in the swollen state it's a typical example of an inorganic gel (Graham, 1864; Hermans, 1949). Starches corn, potato, cassava (Starches) are good gelling substitute instead of conventional gelling agents like agar or gelrite in plant tissue propagation (Nkere *et al*., 2011). Cassava starch is appreciated for

Table 2: Classification and description of gels

Class	Description	Examples
Inorganic	Usually two-phase system	Bentonite magma
Organic	Usually single-phase system	Carbopol, tragacanth
Hydrogel	Organic hydrogel natural and synthetic gums inorganic hydrogel	Methyl cellulose, sodium carboxymethyl cellulose, pluronic, bentonite gel, veegum, silica
Organogel	Hydrocarbon type animal, vegetable fats soap base greases hydrophilic organogel polar nonionic	Petrolatum, mineral oil/polyethylene gel, cocoa butter aluminum stearate with heavy mineral oil gel carbowax bases (PEG ointment)

its paste, clarity, low gelatinization temperature and good gel stability (Kumoro *et al.*, 2010). All of these gels are soft, solid or solid-like materials, which contain substantial's quantities of a liquid.

Flory discussed structural based gel classification (Flory, 1974; Almdal *et al.*, 1993). Mesophases lamellar structures, Covalent polymeric networks; completely disordered, Polymer network formed through physical aggregation predominantly disordered structures. Gels are classified into four categories on the basis of their structure (Table 2). Ease of application non greasy, patient compliance, higher residence time to the skin and better drug release are the advantages of gel preparations (Mathy *et al.*, 2004; Kumar and Himmelstein, 1995; Jones *et al.*, 1999; Rao and Diwan, 1998). Currently gels find own applications like periodontal pockets formation, ophthalmic delivery or vaginal delivery of drugs. Gels are also being used as carrier for solid nano particles. (Warshosaz and Saidian, 2009; Srividya *et al.*, 2001a; Pavelic *et al.*, 2001; Lippacher *et al.*, 2001; Quinones and Ghaly, 2008).

METHOD OF PREPARATION OF GEL

Chemical reaction: In the preparation of sols by precipitation from solution, e.g., Aluminum hydroxide sol precipitated by interaction in aqueous solution of an aluminum salt and sodium carbonate, increased concentrations of reactants will produce a gel structure. Silica gel is another example and is produced by the interaction of sodium silicate and acids in aqueous solution.

Temperature effect: As lower the temperature the solubility of most lyophilic colloids, e.g., gelatin, agar, sodium oleate, is reduced, so that, if cooling a concentrated hot sol will often produce a gel. Similarly to this, some material such as the cellulose ethers shows their water solubility to hydrogen bonding with the water. Increasing the temperature of these sols will break the hydrogen bonding and the reduced solubility will produce gelatin.

Flocculation with salts and non-solvents: Gelatin is a popular collagen derivative primarily used in food, pharmaceutical, photographic and technical products. In foods, gelatin provides a melts-in-the-mouth function and to achieve a thermo-reversible gel property (Herpandi *et al.*, 2011). Gelatin is produced by adding just sufficient precipitant to produce the gel Structure state but insufficient to bring about complete precipitation. It is necessary to ensure rapid mixing to avoid local high concentrations of precipitants. Solutions of ethyl cellulose, polystyrene, etc, in benzene can be gelled by rapid mixing with suitable amount of a nonsolvent such as petroleum ether. The addition of salts to hydrophobic sols brings about coagulation and gelation is rarely observed. However, the addition of suitable proportions of salts to moderately hydrophilic sols such as

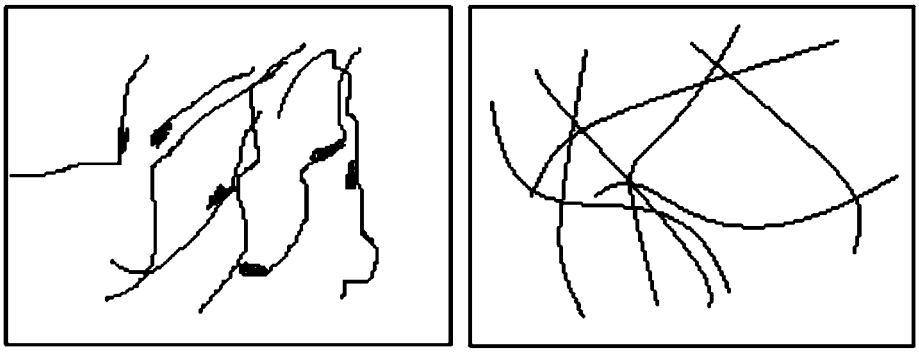

Fig. 2: Different arrangements of particles in gel structure

aluminum hydroxide, ferric hydroxide and bentonite, produces gels. As a general rule, the addition of about half of the amount of electrolyte needed for complete precipitation, as adequate. The gels formed are frequently thixotropic as behavior.

STRUCTURE OF GEL

Elastic gels: Gels of agar, pectin and gelatin are elastic, the fibrous molecules bring at the points of junction but relatively weak bonds such as hydrogen bonds and dipole attraction.

Rigid gels: In contrast to elastic gels, rigid gel can be formed from macromolecules in which the framework is linked by primary valence bonds. e.g., Silica gel.

Thixotropic gel: The term thixotropy describes the property of fluid passing from gel to sol state through agitation. Physical factor to be considered for a gel modifying effects are agitation time, storing time. The bond between particles in these gels is very weak and can be broken by agitation and shaking. The resulting sol will revert back to gel. This is termed as thixotropy. The different possibilities of gel structure are presented systemically in Fig. 2 (Rawlins's, 2003).

INCORPORATION OF NOVEL DRUG DELIVERY SYSTEM INTO GEL

Solid dispersion incorporated gel: Khan *et al.* (2010) developed solid dispersion incorporated gel of aceclofenac for transdermal delivery system using gelling agent as HPMC or Carbopol 940 on rat through abdominal skin. Aceclofenac an analgesic and anti-inflammatory drug used in the treatment of osteoarthritis, rheumatoid arthritis and ankylosing spondylitis (Wanwimolruk *et al.*, 1984). Solid dispersion is the strategy to improve the dissolution and bioavailability of poorly soluble drugs by reducing drug particle size (Badawi *et al.*, 2011; Giri and Sa, 2010; Giri *et al.*, 2010a). Class II compounds should focus on the enhancement of aqueous solubility or dissolution rate (Giri and Sa, 2010). Formulations were evaluated for skin irritation test and *in vivo* efficacy study. The optimized result showed that solid dispersion incorporated HPMC gel have better transdermal delivery for aceclofenac than the solid dispersion incorporated gel of Carbopol 940.

Aejaz *et al.* (2010) described the formulation and *in vitro* evaluation of topical delivery system of an anti-inflammatory drug containing aceclofenac based on the concept of solid dispersion

Table 3: Examples of solid dispersion into gel formulations reported

Drug	Category	Route of administration	Gelling agent	Application	References
Aceclofenac	Analgesic and anti-inflammatory	Transdermal	HPMC, Carbopol 940	Enhance solubility	Khan *et al.* (2010)
Aceclofenac	Analgesic and anti-inflammatory	Topical	HPMC	Improve permeability	Aejaz *et al.* (2010)
Meloxicam	NSAID	Topical	Carbopol 940	Increase dissolution rate of poorly soluble drug	Saleem and Bala (2010)
Ketoconazole	Antifungal agent	Topical	Carbopol 940, Methyl cellulose, Hydroxy propyl methyl cellulose	Better percutaneous absorption	Najmuddin *et al.* (2010)

incorporated gel. The solid dispersion increases the solubility of a drug and successively increases the bioavailability (Seedher and Sharma, 2007). Among the four classes class II drugs shows poor solubility and high permeability (Giri *et al.*, 2010b). The dissolution rate was affected by internal structures of solid dispersions governed by the medium pH (Giri and Tripathi, 2010). Aceclofenac solid dispersion prepared by physical mixture, solvent evaporation method and fusion method using carrier such as PVP, PEG6000 and urea. The higher solubility and release showed in solvent evaporation method. The gelling agent HPMC selected as gel formulation. Formulation was evaluated for pH, viscosity and *in vitro* diffusion study. The result that solid dispersion incorporated gel showed higher permeability and diffusion. Other formulations are described in Table 3.

Liposomal gel: Mitkari *et al.* (2010) developed liposomal gel of fluconazole antifungal drug for topical candidiasis infection using film hydration techniques in factorial design. Liposomal gel prepared in Carbopol® 934 NF and optimized for rheological studies, entrapment and skin permeation study. Liposome gel of fluconazole was showed higher permeability of skin (Hussain *et al.*, 2004).

Jithan and Swathi (2010) studies the improvement of an anti-inflammatory activity of diclofenac sodium on topical delivery based on the concept of liposomal gel as compared to normal gel. Liposome gel were prepared by thin film hydration technique and characterized for *in vitro* drug release, ex vivo permeation and rheological study. The pharmacodynamic studies were performed in male Wistar rats. Diclofenac liposome gel formulation showed better sustained and prolonged anti-inflammatory activity than Diclofenac gel. Other formulations are described in Table 4.

***In situ* gel:** Harish *et al.* (2009) developed *In situ* gel of clotrimazole for oral candidiasis using pH-triggered system containing carbopol 934P (0.2-1.4% w/v) and ion-triggered system using gellan gum (0.1-0.75% w/v) along with HPMC E50 LV. Formulations were evaluated for gelling capacity, viscosity, gel strength, bio-adhesive forces, spreadability, microbiological studies and *in vitro* release. The optimized formulation was able to release the drug up to 6 h. The formulation containing gellan gum showed better sustained release compared to carbopol based gels.

Table 4: Examples of liposome gel formulations reported

Drug	Category	Route of administration	Gelling agent	Application	Reference
Fluconazole	Antifungal	Topical	Carbopol 934 NF	Provide stability	Mitkari *et al.* (2010)
Diclofenac sodium	Anti-inflammatory	Transdermal	Carbopol 934	Improve bioavailability	Jithan and Swathi (2010)
Lidocaine	Local anesthetic	Topical	Carbopol 940	Deliver entrapped drug during on extended period of time	Glavas-Dodov *et al.* (2002)
Tretinoin	Vitamin A	Topical	Carbopol 934	Enhance efficacy	Patel *et al.* (2009a)
Ketoconazole	Antifungal	Topical	Carbopol 940	Increase reaction capacity in skin	Patel *et al.* (2009b)
Ciprofloxacin	Antibacterial	Ocular	Poly (vinyl alcohol) and poly methacrylic acid	Prolong drug release	Budai *et al.* (2007)
Vitamin B12	Water soluble vitamin	Topical	Adenosylcobalamin	Enhanced skin permeability	Jung *et al.* (2011)
Paracetamol	Analgesic and antipyretic	Topical	Carbopol	Enhance the stability	Suriaprabha *et al.* (2009)
Chloramphenicol	Bacteriostatic antimicrobial	Topical	Carbopol 974P	Improve stability	Pavelic *et al.* (2004)
Paclitaxel	Anticancer	Subcutaneous	Poloxamer	Increase dose administration	Dhanikula *et al.* (2008)

Liu *et al.* (2006) describes the formulation and evaluation of an ophthalmic delivery system of an antibacterial agent, gatifloxacin, based on the concept of ion-activated *in situ* gelation. Alginate (Kelton) was used as the gelling agent in combination with HPMC (Methocel E50Lv) which acted as a viscosity-enhancing agent. The rheological behaviors of all formulations were not affected by the incorporation of Gatifloxacin. Both *in vitro* release studies and *in vivo* pre-corneal retention studies indicated that the alginate/HPMC solution retained the drug better than the alginate or HPMC E50Lv solutions alone. These results demonstrate that the alginate/HPMC mixture can be used as an *in situ* gelling vehicle to enhance ocular bioavailability and patient compliance. Other formulations are described in Table 5.

Emulgel: Jain *et al.* (2011) prepared emulsion based gel (emulgel) for topical delivery system on antifungal drug containing miconazole nitrate for fungal infection. The emulsion was prepared and then incorporated into Carbopol used as gelling agent and also the stability of emulsion was increased when prepared emulgel. The prepared gel formulation were optimized on the basis of pH, spreadability rheological study, *in vitro* release and stability studies. The optimized result showed 94.80% release in 24 h and stable for 3 months and also performed microbiological assay using fungal strain.

Jain *et al.* (2010) describes the formulation and evaluation of topical drug delivery system containing an antifungal agent, Ketoconazole based on the concept of emulgel. Emulgel prepared by gelling agent containing Carbopol 934 and Carbopol 940 using factorial designs. The prepared emulgel were evaluated for viscosity, drug release, globule size and skin irritation antifungal study and stability studies. The emulgel showed better release profile than marketed preparation. So it was used for the treatment of fungal infection. Other formulations are described in Table 6.

Table 5: Examples of *in situ* gel formulations reported

Drug	Category	Route of administration	Gelling agent	Application	Reference
Clotrimazole	Antifungal	Oral	Carbopol 934P, HPMC	Improve therapeutic and patient compliance Efficacy	Harish *et al.* (2009)
Gatifloxacin	Antibacterial agent,	Ocular	HPMC	Enhance ocular bioavailability and patient compliance	Liu *et al.* (2006)
Indomethacin	NSAID	Ocular	HPMC, Carbopol	Improved pre-corneal residence time	Pandit *et al.* (2007)
Timolol maleate	Antiglaucoma	Ocular	Carbopol	Prolong residence time	Gupta *et al.* (2007)
Paclitaxel	Antineoplastic	Intratumoral	poly(ethylene glycol) injection-b Polycaprolactone	Prolong action and improve patient compliance	Jauhari and Dash (2006)
Secnidazole	Antibacterial	Vaginal	Gellan gum	Better stability and longer residence time	Narayana *et al.* (2009)
Ofloxacin	Antibacterial	Ophthalmic	Carbopol 940	Stable	Srividya *et al.* (2001b)
Linezolid	Antibacterial	Ophthalmic	Carbopol	Increase residence time	Swamy *et al.* (2008)
Levofloxacin	Antibacterial	Ocular	Carbopol 940, HPMC	Improve bioavailability and longer residence time	Mohanambal *et al.* (2011)
Clarithromycin	Antimicrobial	Oral	Gellan gum	Prolong residence time and enhance stability	Bhimani *et al.* (2011)
Amoxicillin	Broad spectrum antibiotic	Oral	Gellan gum	Prolong residence time	Rajnikant *et al.* (2007)
Diclofenac sodium	NSAID	Ophthalmic	Carbopol 940	Increase patient compliance	Asasutjarit *et al.* (2011)
Baicalin	Anti-inflammatory and anticataract	Ophthalmic	Carbopol 974P	Better stability	Wu *et al.* (2011)
Ciprofloxacin	Antibacterial	Ocular	Poloxamer	Good stability	Balasubramaniam and Pandit (2003)
Dimenhydrinate	Antihistamine	Nasal	Gellan gum	Increase permeation rate	Mahajan *et al.* (2009)
Pheniramine and phenylephrine	Antihistaminic	Nasal	Xanthan gum, HPMC	Prolonged residence time	Mehta *et al.* (2009)

Solid lipid nanoparticles incorporated gel: Liu *et al.* (2008) the solid lipid nanoparticles using Carbopol gel as gelling agent containing triamcinolone acetonide acetate (glucocorticoid compound) for transdermal iontophoretic delivery. Solid lipid nanoparticles formulation was prepared by high pressure homogenization technique and Carbopol gel added to provide stability. The formulation characterized for particle size. Zeta potential, rheological. Electrical conductivity, *in vitro* release, stability, transdermal iontophoretic study and HPLC analysis. These result demonstrated that good stability and rheological study and high electrical conductance in solid lipid nanoparticles incorporated gel as a carrier for transdermal iontophoretic delivery system. The mechanism of increased bioavailability is not known but assumed to lymphatic transport of the drug either alone or along with the lipid carrier (Amarji *et al.*, 2007).

Table 6: Examples of emulgel formulations reported

Drug	Category	Route of administration	Gelling agent	Application	Reference
Miconazole nitrate	Antifungal	Topical	Carbopol	Increase stability	Jain *et al.* (2011)
Ketoconazole	Antifungal	Topical	Carbopol 934 and carbopol 940	Enhance stability	Jain *et al.* (2010)
Diclofenac sodium	NSAID	Topical	Carbopol 934P	Prevent microbial attack	Vijayabhanu *et al.* (2011)
Sodium metabisulphite and glutathione	Antioxidant	Oral	HPMC	Stability of active substance	Maia *et al.* (2006)
Flurbiprofen	Antiinflammatory	Buccal	Pemulen 1621 TR-1)	Prolonged retention time	Perioli *et al.* (2008)
Chlorphenesin	Antifungal and antibacterial	Topical	HPMC, carbopol 934	Higher drug release	Mohamed (2004)
Itraconazole	Antifungal	Topical	Carbopol 934, carbopol 940	Increase stability	Deveda *et al.* (2010)
Mefenamic acid	NSAIDs	Topical	-	-	Khullar *et al.* (2012)
Tetra hydropalmatine	Alkaloid	Transdermal	Carbopol® 971P	-	Li *et al.* (2011)
Ketorolac trometamol	NSAID	Transdermal	-	-	El-Setouhy and El-Ashmony (2010)
Clobetasol	Corticosteroid	Topical	-	-	Badilli *et al.* (2011)
Kanamycin	Aminoglycoside Antibiotic	Topical	Silica [K-SG]	Showed good technological characteristics for its application to the skin	Lopez-Cervantes *et al.* (2009)
Benzydamine	NSAIDS	Vaginal	Carbopol 971P	Enhance skin permeation	Perioli *et al.* (2009)

Gaddam and Aukunuru (2010) formulated and evaluated solid lipid nanoparticles incorporated gel of anti-inflammatory drug containing Diclofenac sodium for topical application. Solid lipid nanoparticles prepared by hot homogenization and incorporated into carbopol gel. The formulations were evaluated for *in vitro* drug release, viscosity ex vivo permeation and pharmacodynamic studies on male Wistar rats. The *in vivo* and *in vitro* studies in solid lipid nanoparticles incorporated gel showed drug release for 24 h. The result showed higher the systemic delivery of solid lipid nanoparticles in gel with Diclofenac sodium. Other formulations are described in Table 7.

Microemulsion gel: Suthar *et al.* (2009) developed microemulsion based gel of Tretinoin in topical delivery system for the treatment of acne. The microemulsion based gel was prepared by using surfactant, cosurfactant and oil and gel was prepared by using Carbopol 934 as gelling agent. The microemulsion based gel was characterized for droplet size, zeta potential, permeation, rheological and stability studies. The droplet size of formulation was found range between 10-100 nm and zeta potential of oil between -7.02-0.044 mV. The result showed that higher permeability and better stability. The nanoparticles synthesized in the microemulsion containing PVP exhibit higher catalytic efficiency compared with those prepared in the microemulsion without a polymer and PEG microemulsion systems (Yadav *et al.*, 2008).

The influence of the vehicle on the release and permeation of Fluconazole, a topical antifungal drug dissolved in Jojoba oil was evaluated by Ellaithy and El-Shaboury (2002). The results of

Table 7: Examples of Solid lipid nanoparticles incorporated gel formulations reported

Drug	Category	Route of administration	Gelling agent	Application	Reference
Triamcinolone acetonide acetate	Glucocorticoids compound	Transdermal drug delivery	Carbopol	Good stability and rheological property	Liu *et al*. (2008)
Diclofenac sodium	Anti-inflammatory	Topical	Carbopol 934	Better systemic delivery	Gaddam and Aukunuru (2010)
Valdecoxib	Anti-inflammatory	Topical	-	Faster onset of action and prolonged delivery	Joshi and Patravale (2006)
Calixarene	-	-	Carbopol 980, carbopol 2020, hyaluronic acid and xanthan	-	Shahgaldian *et al*. (2003)
Ascorbyl palmitate	-	Dermal	-	Viscosity	Teeranachaideekul *et al*. (2008)

Table 8: Examples of Microemulsion gel formulations reported

Drug	Category	Route of administration	Gelling agent	Application	Reference
Tretinoin	Vitamin A	Topical	Carbomer 934	Increase the Viscosity	Suthar *et al*. (2009)
Fluconazole	Antifungal	Vaginal	Cetyl palmitate	Widest zone of inhibition	Ellaithy and El-Shaboury (2002)
Fluconazole	Antifungal	Vaginal	Carbopol® ETD 2020	Faster onset of action	Bachhav and Patravale (2009)
Nonoxynol-9	Microbicides	Vaginal	Rhodigel	Improve vaginal bioavailability	D'Cruz *et al*. (2001)
Nonoxynol-9	Antimicrobial	Vaginal	-	Improve bioavailability	D'Cruz and Uckun (2001)
Vitamins C and E	Antioxidant	Topical	Carbomer	Increase penetration into the skin	Rozman *et al*. (2009)
Ibuprofen	NSAID	Topical	Xanthan gum	Improve the viscosity	Chen *et al*. (2006)
Zolmitriptan	Antimigraine agent	Nasal	Triggered gel formation	enhanced bioavailability with rapid onset of action	Shelke and Devarajan (2007)

in vitro drug release and its percutaneous absorption showed that the highest values from gel microemulsion were assured. The rheological behavior of the prepared systems showed pseudoplastic (shear-thinning) flow indicating structural breakdown of the existing intermolecular interactions between polymeric chains. The antifungal activity of Fluconazole showed the widest zone of inhibition with gel microemulsion. The gel microemulsion is an excellent vehicle for Fluconazole topi-cal drug delivery. The antifungal activity of Fluconazole showed the widest zone of inhibition with gel microemulsion. The gel microemulsion is an excellent vehicle for fluconazole topical drug delivery. Other formulations are described in Table 8. The permeation study shows the

Table 9: Examples of hydrogel formulations reported

Drug	Category	Route of administration	Gelling agent	Application	Reference
Nicotine	Stimulant	Transdermal	Agar	Control both its delivery rate and the pH	Conaghey *et al.* (1998)
Loratadine	Antihistamine	Topical	Carbopol 980	Prolong drug release	Capkova *et al.* (2005)
Diclofenac sodium	Anti-inflammatory	Oral	Sodium alginate	Prolong release time and improve drug efficacy	Qin and Andaiqinwang (2009)
Silymarin	Antioxidant	Oral	Sodium alginate	Improve dissolution and bioavailability	El-Sherbiny *et al.* (2011)
Bovine serum albumin	Protein	Oral	HPMC	Increase swelling ability	Nochis *et al.* (2008)
Prazocine hydrochloride	Anti-hypertensive	Transdermal	Sodium alginate	Improve bioavailability	Raghvendra *et al.* (2010)

effectiveness of the delivery system and a proper selection of the methodology will further improve the study and for the same mechanistic permeation studies with eschar tissue in case of antimicrobial drugs used for burn wounds (Zadeh *et al.*, 2010).

Hydrogel: Conaghey *et al.* (1998) investigated the iontophoretically assisted across in *in vitro* membrane of nicotine loaded carrier based on the concept of hydrogel of an ion exchange resin. Agar was used as gelling agent. In this nicotine had been bound. The hydrogel evaluated for bead size and degree of cross linking and drug concentration effects. This studied significantly advantageous over comparable to simple hydrogel and also shown that control both its iontophoretic delivery and pH of carrier. Terbinafine hydrochloride is an antifungal agent which is used to prepare hydrogel for the comfort of the patient; these hydrogel can be used for local therapeutic transdermal delivery application of cationic drugs (Ahmad *et al.*, 2003).

Capkova *et al.* (2005) describes the formulation and evaluation of topical delivery system of an antihistaminic agent, Loratadine, based on hydrogel and Carbopol 980 is used as carrier in the concentration of 0.5, 0.8 and 1.0%. The objective of this study to determine the maximum concentration of Carbopol 980 for the development of hydrogel. The hydrogel optimized for pH, rheological and drug release study. The result suggests that 0.5% Carbopol 980 was highest concentration for the formulation of hydrogel. Other formulations are described in Table 9.

Marketed preparation of gel: We were survey various category of drug which are formulated as gel in that most popular are trolamine salicylate (NSAID) and it is used for muscle soreness and it is available in market like sunscreen, analgesic cream and cosmetics. Cansema (escharotic) and it is used for cures for skin cancer and marketed product is topical paste. Similarly various category of drugs which are formulated as gel are described in given (Table 10) with their use and marketed formulation.

Denouement: Gels are transparent semi-solid formulation containing a high ratio of gelling agent. These system forms a three-dimensional structure. Incorporation of gel in novel drug delivery system provides increase in skin permeation, stability, rheological property. Topical administration is becoming an important route for drug administration because of its local effects on infected part of the skin.

Table 10: Available marketed preparation of gels reported

Drug	Category	Uses	Marketed formulation
Trolamine salicylate	NSAID	Muscle soreness	Sunscreens, analgesic creams and cosmetics
Cansema	Escharotic	"Cures" for skin cancer	Topical paste
Corticosteroid	Steroid hormone	Regulation of inflammation	Use topically on the skin, eye and mucous membranes
Caffeine	Xanthine alkaloid	Androgenic alopecia	Shampoos and cosmetics
Minoxidil	Antihypertensive	Both men and women to treat hair loss	Topical solution
Chloramphenicol	Bacteriostatic, antimicrobial	Used topically for eye infections	Ointments and eye drops
Heparin	Anticoagulant	Atrial fibrillation, Cardiopulmonary, bypass for heart surgery	Parenterally
Vitamin k	Fat soluble vitamins	To treat rosacea, hyper pigmentation	Cream
Fluconazole	Triazole antifungal	Prevention of superficial and systemic fungal infections	Topical
Ibuprofen	Nonsteroidal anti-inflammatory	Treatment of acne	Topical gel form
Ketamine	Opioid receptors	Nerve pain	Cream, gel, or liquid for topical application
Lidocaine	Local anesthetic	Relieve itching	Topically

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