An Overview on Emulgel

Ghanshyam potdar [1], Poonam Kamate [2], Pranjal Chougule [3], Nilesh Chougule [4].
[1,2]*Stuendts, Ashokrao Mane Institute of Pharmacy, Ambap, Kolhapur-416112*
[3]*Assistant Professor, Ashokrao Mane Institute of Pharmacy, Ambap, Kolhapur-416112*
[4]*Principal, Ashokrao Mane Institute of Pharmacy, Ambap, Kolhapur-416112*

Abstract- As compaire to other semisolid dosage form gels or other topical dosage form shows advantages in pharmaceutical preprations and cosmetics. Medications in gel form usually have a faster rate of release than those in topical ointments and creams. Term "Emulgel" describes a combination of gel and emulsion. To alleviate symptoms or cure diseases, a topical drug delivery device applies the medicine directly to the skin. One big drawback of the gels is that they can't transport hydrophobic drugs. The Emulgels are able to overcome it. In dermatology, emulgels are advantageous for numerous reasons, such as their thixotropic properties, lack of grease, ease of spreading, detachability, emollient properties, water solubility, prolonged shelf life, biocompatibility, transparency, and aesthetic appeal. Another important consideration is the possibility of extending the drug release of hydrophilic medications without the use of emulgel.

Keywords: Emulgel, Viscosity, Stability, Spreadability, Skin Absorption, Active Ingredients

INTRODUCTION

Topical drug administration refers to the localized delivery of medication through the skin, vaginal, ophthalmic, and rectal channels to any part of the body. The ability to circumvent hepatic metabolism is one benefit of topical medication delivery. Additionally, it helps in evading the risks and hassles of intravenous therapy. Different consistencies of topical formulations, including liquid, semisolid, and solid, are created. When a medicine that is hydrophobic is administered topically, it fails. Excipients are employed in large quantities in every composition containing active substances. Emulgel is one example of a combination of formulations that can occasionally be used in conjunction with one another to improve medication delivery. It is a blend of gel and emulsion. [1].

Starting in the mid-1980s, emulsion gels began to play a larger role in development of topical semisolid pharmaceutical dosage formulations. One reason emulsion systems are so popular as a dosage form for medicine is their extensive usage in dermatological formulae. Emulgels are made by combining an emulsion O/W or W/O with a gelling agent. This mixture then forms a gelled consistency. [2]

The emulsion also serves as a mechanism for the controlled release of medications by facilitating the passage of drug particles from the internal to the exterior phase, which in turn allows them to soak into the skin over time. A regulated delivery of the medicine is accomplished by passing it through the inner layers of the skin, which act as a reservoir for drug. Gel's ability to gradually release microscopic medicine particles is due to its crosslinked network. Because of its mucoadhesive properties, it remains in touch with the skin for an extended duration following pharmaceutical administration. [3]

If the topical administration of a medicine that is not extremely water-soluble is an issue, emulgels may be the way to go. For medications that are hydrophobic or have limited solubility in water, it has also shown to be an effective and stable carrier. [4,5,6]

Emulgel types:

Microemulsion:

A microemulsion consists of an isotropic mixture of a transparent, thermodynamically stable surfactant and a biphasic oil-in-water systemic stabiliser. Sizes of droplets vary between 10 and 100 nm and do not combine. It contains oil, surfactant, water, and co-surfactant in certain ratios. A few distinguishing features of microemulsions are capability to dissolve water-and oil-soluble compounds, a large interfacial region, and extremely low interfacial tension. The components of microemulsion may allow for a higher rate of medication penetration by decreasing diffusion

barrier in stratum corneum. Because of their low viscosity, microemulsions have limited utility in the pharmaceutical sector because of their poor skin retention ability. The addition of gelling chemicals such as guar gum, Carbopol 940, and HPMC K100M is done to overcome this constraint. [7,8,9]

Nanoemulgel :

Because it comprises surfactant and cosurfactant molecules, a nanoemulsion is thermodynamically stable and appears as a clear oil-water dispersion with globule diameters between 1 and 100 nm. Combining emulsion and gel is what the name "Nanoemulgel" means. Medications in nanoemulsion form are able to reach deeper layers of skin than those in more conventional formulations like emulsions and gels. In both laboratory and living organism studies, the nanoemulsion demonstrates improved transdermal and dermal transport capabilities. Because of its small globule size and high loading capacity, the drug readily penetrates the skin and has a short half-life of therapeutic effect.

Macroemulsion gel:

Emulgel with particles larger than 400 nm in the emulsion droplet size. The individual droplets are clearly visible under a microscope, but they are physically invisible. Despite their thermodynamic instability, macroemulsions can be stabilized with the aid of surface-active agents.

Advantages:

1 The use of hydrophobic medications
2. An increased loading capacity
3. Enhanced steadiness
4. Regulated discharge
5. Lack of heavy sonication
6. Preventing metabolism via first pass
7. Preventing gastrointestinal intolerances
8. More specialized for a given location
9. Increased adherence from patients
10. Easy to use and convenient [10]

Disadvantages:

1. Itchy skin, also known as contact dermatitis
2. Possibility of adverse responses
3. Skin penetrability is low for some drugs.
4. Drugs with large particles have a hard time penetrating and being absorbed by the skin.
5. A bubble that forms while emulgel is being made [11]

Drug absorption affecting factor:

(A) Physiological Factors:

1. Density of sweat glands.
2. Skin pH.
3. Density of hair follicles.
4. Skin thickness.
5. Hydration of skin.
6. Blood flow.
7. Lipid content.

(B) Physiochemical Factors:

1. Molecular weight
2. Degree of ionization
3. Partition coefficient.
4. Effect of vehicles. [12,13,14]

8.Properties of additives:

1. They should be nontoxic.
2. They should be easily available.
3. They should be cheap.
4. They do not be contraindicated.
5. They should chemically and physically be stable.

Various ingredients of Emulgel formulation:

Aqueous material:

The aqueous phase of emulsion is formed by this. As a rule, water is employed.

Oils:

They are responsible for making the oily part of the emulsion. A number of oil physicochemical parameters, including molecular volume, polarity, and viscosity, are important in defining the final emulsion's droplet size, drug solubility, and the efficacy of the emulsification, microemulsification, and nanoemulsion processes. Consequently, the oil phase is of utmost significance during the formulation process. As a viscous phase, the oil that possesses the greatest solubilizing potential for the chosen drug candidate is typically favored when preparing emulsions, microemulsions, and nanoemulsions. This facilitates the achievement of maximum drug absorption. Thus, emulsions possessing desirable properties are frequently selected as the viscous phase. The following oil phases are utilized in the formulation of emulgel: balsam oil, castor oil, [15], birch oil, [16], isopropyl myristate, [17, 18, 19],

myrrh oil, [20,21,22], rose hip oil[23], and wheat germ oil [24,25]. [26,27,28]

Emulsifiers:

In order to control stability and emulsification process, emulsifiers are utilized. Due to their inherent thermodynamic instability, the stability of the emulsion can be enhanced through the addition of the appropriate emulsifying agent. Emulsions of water and oil are made with mineral oils, such as liquid paraffin, since their hydrocarbon light-burning (HLB) values are less than 8. On the other hand, nonionic surfactants (spans, tweens) and other surfactants with HLB values more than 8 make up o/w emulsions. When mixtures of span 20 and tween 20 are utilized as opposed to either system alone, the emulsion is more stable. [29]

Permeation enhancer:

There are chemicals called penetration boosters that support a penetrant get through skin by temporarily breaking down skin's barrier to absorption. Ideally, these chemicals should be cheap, have no taste, color, or smell, not be harmful, and not affect how drugs work. They should also be good at dissolving things, not irritate or poison, and work well with the drugs and excipients. The enhancer shouldn't make the body lose electrolytes, bodily fluids, or other naturally occurring substances, and as soon as it's taken off, the skin should immediately return to its protective function. Some of the penetration boosters that are used in emulgel are oleic acid [30], clove oil [31], menthol [32], and others.

Gelling Agents:

Emulgel is made by adding emulsion to a gel base that has been made using a gelling agent. These substances are known as thickening agents because they develop a gel-like structure and expand when exposed to water, making any dose form more substantial. [33] A system becomes thixotropic when a gelling agent is added to it.on page 34 Because it demonstrated a better drug release rate, HPMC-based Emulgel was determined to be superior to Carbopol-based Emulgel. The highest in-vitro and in-vivo performance, along with enhanced mucoadhesivity that extended the drug's residence time, made NaCMC-based emulgels ideal for vaginal use. Emulgel based on HEC exhibited favorable rheological properties and drug release profiles with minimal mucoadhesion. A buccal-administered emulgel containing pemulen.

S.no	Gelling agents	Concentration used (%w/w)	Pharmaceutical Adaptability	Active pharmaceutical ingredient
1	Sodium CMC	3-4%	Stand autoclaving hence suitable for sterile gels	Benzydamine
2	Carbopol-934	1%	Provide controlled release of API incorporated	Chlorphenesin
3	Carbopol-940	1%	Because of high viscous gel, provide controlled release of API incorporated	Mefenamic acid
4	HPMC	2.5%	Having good stability, microbial resistance	Clorphenesin
5	Combination of HPMC & Carbopol	1.2%	Combination improve stability	Ketorolac, clotrimazole
6	Pluronic® F127	1-3%	Good clarity and better solubility in cold water	Piroxicam
7	Pemulen	0.1-0.4%	Provide rapid release of oil phase, excellent stability	Flurbiprofen

PREPARATION OF EMULGEL

As a result of combining gel and emulsion, emulgel is created. After being prepared independently, the gel and emulsion are combined.

The emulsion is made by dissolving the oil phase and mixing it with the water phase. After that, a gelling agent is added to get the gel ready. Following their preparation, the gel and emulsion are combined by gently swirling them together. Some of the compounds that make up the oil phase are liquid paraffin, castor oil, clove oil, and others. Both alcohol and water are utilized in the aqueous phase. [35]. To make the watery phase, just mix Tween 80 with water. To make the oily phase, just mix propylene glycol with paraben. After dissolving the medicine in ethanol, the two components are mixed while being vigorously swirled. Water with a pH of 6.0 to 6.5 is

then used to dissolve the polymers. The emulsion and gel are made independently and then mixed to make emulgel.

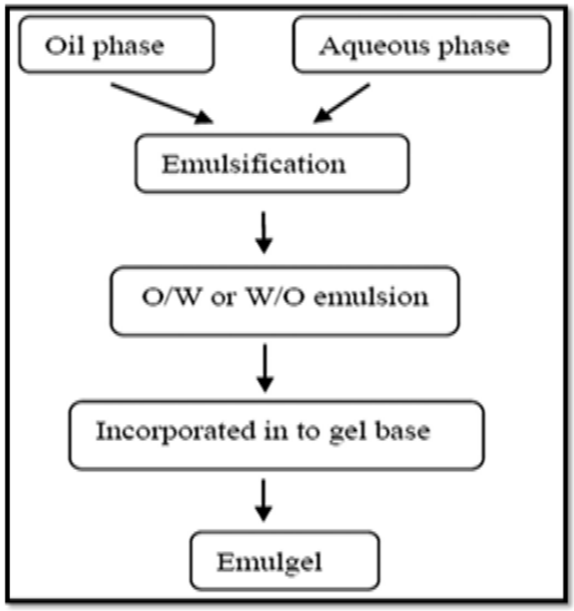

Fig. 4: Flow chart of emulgel preparation [36].

FORMULATION OF EMULGEL:

While making emulgel, you'll need the following ingredients, one of which is a medicine

Vehicle:

The vehicle you use should adhere to the specifications laid out in the Pharmacopeias.

Aqueous material:

Water, alcohol, and other aqueous phases are utilized.

Oil:

Emulsion preparation involves the use of oils. Paraffin and mineral oils can be used singly or in tandem [37].

Emulsifiers:

The term "emulsifier" refers to substances that help create an emulsion. A few examples are stearic acid, sodium stearate, span 80, and tween 80.

Gelling agents:

In order to make gels, which improve the consistency of the preparation, gelling agents are utilized.

Penetration enhancers:

To improve drug absorption to the skin, penetration enhancers are used. [38].

MARKETED FORMULATION OF EMULGEL:

S. no.	Marketed Formulation	API	Manufacturer	Use
1.	Diclobar emulgel	Diclofenac diethyl amine	Barakat Pharma	Anti-inflammatory, analgesic
2.	Voltaren emulgel	Diclofenac diethyl ammonium	Novartis Pharma	Anti-inflammatory
3.	Miconaz-H-emulgel	Miconazole nitrate, Hydrocortisone	Medical union Pharmaceuticals	Topical corticosteroid and antifungal
4.	Diclomax emulgel	Diclofenac sodium	Torrent Pharma	Anti-inflammatory
5.	Levorag emulgel	Hibiscus, licorice	THD Ltd. natural extracts	Emollient

Table: Marketed formulation of emulgel [39]

EVALUATION TECHNIQUES

- Physical examination:

This is where color, uniformity, stability, and phase separation are checked. [40].

- Spreadability:

The emulgel's "slip" and "drag" characteristics verify its spreadability. A pulley at one end of the device, which entails of a wooden block, is used to measure spreadability. A ground glass is fixed in the block. It is topped with two grams of emulgel and sandwiched between two glass slides. It is weighted with one kilogram and its spreadability is evaluated.

- Determination of pH:

A digital pH meter can be used to determine it. To check the pH three times, dip the pH meter into the emulgel.

- Rheological study:

At 25 ºC, the viscosity is measured in rheological studies. Cone and plate viscometers are tools utilized. [41].

- In vitro drug release study:

Using a Franz diffusion cell, it is accomplished. Identifying medication release is aided by it. [42].

❖ Microbiological assay:

The ditch plate technique is employed for this purpose. This approach is used to assess antimicrobial or antifungal activity.

Quick investigations into stability: This follows the standards set out by the ICH. The stability test lasts for three months in a hot air oven set at 37 ± 2 ºC, 45 ± 2 ºC, and 60 ± 2 ºC [43].

❖ Drug content:

Ultraviolet spectroscopy is used to find the amount of medication. This equation is utilized:

$$\text{Drug content} = (\text{Concentration} \times \text{Dilution factor} \times \text{Volume taken}) \times \text{Conversion factor}$$

❖ Globule size and distribution in emulgel:

Malvern Zetasizer determines it. To ascertain value, the emulgel is dissolved in water, stirred, and placed into the equipment.

❖ Centrifugation study:

Stability of emulgel can be evaluated using this technique. A week of preparation is required before it is completed. The minicentrifuge was spun at 3000 rpm for 30 minutes in order to conduct this study.

❖ Swelling index:

Separately, put 10 milliliters of 0.1 N NaOH into a 50 milliliter beaker and transfer 1 gram of emulgel on a piece of porous aluminum foil. The samples are thereafter taken out at various intervals and weighed again. The formula for the swelling index is;

$$\text{Swelling index (SW)} \% = [(Wt\text{-}Wo)/Wo] \times 100$$

Where,

Wo = Original weight of emulgel at zero time.

Wt = Weight of swollen emulgel after time t,

❖ Skin irritation test:

Being a topical formulation, this test is absolutely necessary for preparation. The test is conducted on the skin of the animal. Following the application of emulgel to the skin, the animals are returned to their enclosures. The animals are evaluated again after a day. Then, using tap water, remove the emulgel from the area.

❖ Stability studies:

The stability of the emulgel was tested after it was packed in aluminum collapsible tubes and kept under harsh conditions

CONCLUSION

The more recent development of topical drug delivery systems has made emulgel an ideal choice for administration of hydrophobic drugs as well as those containing both hydrophilic and hydrophobic components. To increase patients' adherence, topical medicine delivery will be heavily used. Emulgel will become more popular as a medication delivery strategy due to its superior spreadibility, adherence, viscosity, and extrusion compared to other approaches.

REFERENCE

[1] Purushottam Sonaje Sumeet, Bhaskarrao Gondkar Sheetal, Bhandudas Saudagar Ravindra., 2013. Gellified Emulsion: A New Born Formulations For Topical Delivery of Hydrophobic Drugs A Review, World Journal of Pharmacy and Pharmaceutical Sciences, 3(1), pp 233-251.

[2] Mohamed MI: Optimization of chlorphenesin emulgel formulation. AAPS J.2004; 6: 26.

[3] Alexander A, Ajazuddin, Tripathi DK, Vrema ST, Maurya J, Patel S: Mechanism responsible for mucoadhesion of mucoadhesive drug delivery system: a review. Int. J. Appl. Biol. Pharm. Technol.2011; 2: 434–445.

[4] Dickinson E: Hydrocolloids as emulsifiers and emulsion stabilizers. Food Hydrocolloids 2009; 23: 1473–1482.

[5] Jain A, Gautam SP, Gupta Y, Khambete H, Jain S: Development and characterization of ketoconazole emulgel for topical drug delivery. Pelagia Res. Libr. 2010; 1: 221–231.

[6] Ajazuddin A, Alexander J, Khan TK, Giri DK, S. Saraf ST: Advancement in stimuli triggered in situ gelling delivery for local and systemic route. Expert Opin. Drug Deliv.2012; 9: 1573–1592.

[7] Sharma A K, Tarun Garg, Goyal A K, Rath G. Role of microemulsion in advance drug delivery. Informa healthcare. 2014; 4: 1177-1185.

[8] Anand K, Ray S, Rahman M, Shaharya M A, Bhowmik R, Bera R. Nano-Emulgel: Emerging as a Smarter Topical Lipidic Emulsion-based Nanocarrier for Skin Healthcare Applications. Recent Patents on Anti-Infective Drug Discovery. 2019; 14(1): 16-35.

[9] Hyma P, Jahan N, Raheemunissa, Sreelekha G, Babu K. Emulgel: A Review. International Journal of Pharmaceutical Archive. 2014; 2(3): 459-467.

[10] Jain NK, 2004. Progress in controlled and novel drug delivery st systems. New Delhi: CBS publishers and distributors, 1, pp 319-20.

[11] Hardenia A, Jayronia S, Jain S, 2014. Emulgel: An emergent tool in topical drug delivery. International Journal of Pharmaceutical Science and Research, 5, pp 1653-60.

[12]. Ranga PM, Sellakumar V, Natarajan R, Mohan KK. Formulation and In-vitro evaluation of ciprofloxacin-loaded topical emulgel. Int J Pharm Chem Sci 2012;1:237-42.

[13]. Singla V, Saini S, Rana AC, Singh G. Development and evaluation of topical emulgel of lornoxicam using different polymer bases. Int Pharm Sci 2012;2:36-44.

[14]. Narendran H, Koorapati S, Mamidibathula L. Formulation and evaluation of Aceclofenac-lycopene transemulgel. World J Pharm Res 2013; 2: 1036-45

[15] Beitz JM: Heparin induced thrombocytopenia syndrome bullous lensions treated with trypsin-balsam of peru-castor oil ointment: a case study. Ostmony Wound Manage. 2005; 51: 52–54.

[16] Jager S, Laszczyk MN, Scheffler A: A preliminary pharmatokinetic study of Betulin, the main pentacyclic triterpene from extract of outer bark of birch. Molecules 2008; 13: 3224–3235.

[17].Maissa C, Guillon P, Simmons P, Vehige J: Effect of castor oil emulsion eye drops on tear film composition and stability. Contact Lens Anterior Eye 2010; 2: 76–82.

[18].Zhu K, Zhou H, Qian H: Antioxidant and free radicalscavenging activities of wheat germ protein hydrolysates (WGPH) prepared with alcalase. Process. Biochem.2006; 41:1296–1302.

[19] Lawrence MJ, Rees GD: Microemulsion based media as novel drug delivery systems. Adv. Drug Deliv. Rev2000; 45: 89–121.

[20] Podlogar F,Gasperlin M, Tomsic M, Jamnik A, Rogac BM:Structural characterization of water-tween 40/Imwitor 308-isopropyl myristate microemulsions using different experimental methods. Int. J. Pharm. 2004; 276:115–128.

[21] M. Tomsic M, Podlogar F, Gasperlin M, Rogac BM, Jamnik A: Water-Tween 40/Imwitor-isopropyl myristate microemulsions as delivery system for ketoprofen: small angle X-ray scattering study. Int. J. Pharm. 2006; 327:170–177.

[22] Nandi I, Bari M, Joshi H: Study of isopropyl myristate microemulsion systems containing cyclodextrins to improve the solubility of 2 model hydrophobic drugs. AAPS Pharm. Sci. Technol. 2003; 4: 71–79.

[23] Tipton DA, Lyle B, Babich H, Dabbous MK: In vitro cytotoxic and anti-inflammatory effects on human gingival fibrobast and epithelial cells. Toxicol. Vitr. 2003; 17: 301– 310.

[24] Machmudah S, Kawahito Y, Sasaki M, Got M: Supercritical carbon dioxide extraction of rosehip seed oil: fatty acid composition and rose hip optimization. J. Supercrit. Fluids 2007:41: 421–428.

[25] Kirkeskov B, Christensen R, Bugel S, Bliddal H, Christensen LP, Anders JR: The effect of rose hip on plasma antioxidative activity and C-reative protein in patients with rheumatoid arthritis and normal control: a prospective cohort study. Phytomedicine2011; 18: 953– 958.

[26] Karabacak M, Kanbur M, Eraslan G, Sanca ZS: The antioxidant effect of wheat germ oil on subchronic comaphos exposure in mice. Ecotoxicol. Environ. Saf. 2011; 74: 2119–2125.

[27] Malecka M: Antioxidant properties of unsaponificable material extracted from tomato seeds, oat grain and wheat germ oil. Food Chem. 2002; 79: 327-300.

[28] Jing F, An X, Shen W: The characteristics of hydrolysis of triolein catalyzed by wheat germ lipase in water in oil microemulsions. J. Mol. Catal. B Enzym.2003; 24–25: 53– 60.

[29] Vilasau J, Solans C, Gómez MJ, Dabrio J, Mújika-Garai R, Esquena J: Phase behaviour of a mixed ionic/nonionic surfactant system used to prepare stable oil-in-water paraffin emulsions. Colloids Surf., A Physicochem. Eng. Asp.2011; 384: 473–481.

[30] Baibhav J, Singh G, Rana AC, Saini S: Development and Characterization of Clarithromycin Emulgel for topical delivery. IJDDR, 2012; 4(3): 310-323.

[31] Khullar R, Kumar D, Seth N, SainiSeema: Formulation and evaluation of mefenamic acid

emulgel for topical delivery. Saudi Pharmaceutical Journal, 2012; 20: 63–67.

[32] Prajapati Mehulkumar N, Patel M R, Patel K R and Patel N M: Emulgels: a novel approach to topical drug delivery. IJUPBS 2013; 2(1): 134-148.

[33] Patel RP, Patel G, Baria A: Formulation and evaluation of transdermal patch of aceclofenac. Int. J. Drug Del. 2009; 1: 41 – 51.

[34] Baibhav J, Singh G, Rana A. C., Saini S, Singla V: Emulgel: A Comprehensive Review on The Recent Advances In Topical Drug Delivery, International Research Journal of Pharmacy.2011; 2(11); 66-70.

[35] Anil R. Phad, Nandgude Tanaji Dilip, R. Sundara Ganapathy, 2018. Emulgel: A Comprehensive review for Topical Delivery of Hydrophobic Drugs. Assian Journal of Pharmaceutics, 12 (2), pp 382 -393.

[36] Singla et al, 2012. Emulgel: a platform for topical drug delivery. International Journal of pharmaceutical and biological sciences, 3, Issue 1

[37] Pant S, Badola A, Baluni S, Pant W, 2015. A review on emulgel novel approach for topical drug delivery system. World Journal of Pharmacy and Pharmaceutical Sciences, 4, pp 1728-43.

[38] Mortazavi SA, Aboofazeli R, 2003. An Investigation into the Effect of VariousPenetration Enhancers on PercutaneousAbsorption of Piroxicam. Iranian Journal of Pharmaceutical Research, pp 135-140

[39] Ojha A, Ojha M, Satheesh Madhav N V, 'Recent Advancement in Emulgel: A Novel Approach for Topical Drug Delivery, *International Journal of Advances in Pharmaceutics*, 2017; **21**.

[40] George Eby and Mathews Manju Marai, 2014. Formulation and Evaluation of Topical Gel containing Hair Growth Promoters for the Treatment of Androgenic Alopecia A Research Article, Bulletien of Pharmaceutical Research, 4(1), pp 1-8.

[41] Masmoudi H, Piccerelle P, Le Dréau Y, Kister J, 2006. A rheological method to evaluate the physical stability of highly viscous pharmaceutical oil-in-water emulsions. Pharm Res.,23(8), pp 1937–47.

[42] Subranayam N, Ghosal SK, Moulik SP, 2005. Enhanced In Vitro Percutaneous Absorption and In Vivo Anti-Inflammatory Effect of a Selective Cyclooxygenase Inhibitor Using Microemulsion. Drug Development and Industrial Pharmaceutics,1(3), pp 12-19

[43] Rutrer N, 1987. Drug absorption through the skin: a mixed blessing. Arch Dis Child. 62, pp 220-221