IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

An overview: preparation of emulgel by using mefenamic acid

Author:- Miss.shaikh.s ,Mr. Joshi. D. A, Dr. Bavage. S. B, Miss madhuri. S

Department of pharmaceutics, latur college of pharmacy Hasegaon, tq. Ausa, District. Latur,413512, Maharashtra. India

Abstract:

Emulgel are currently topic of attention to pharmaceutical scientists due to their high potential to act as drug delivery vehicle by incorporating high range of drug molecules. Emulgel due to lack of insoluble excipients and excessive oily bases it demonstrate better drug release as compared to other topical drug delivery system. The combined form of gel and emulsion referred as emulgel. Emulgel is promising drug delivery system of hydrophobic drugs it had dual release control system that is gel and emulsion. It is highly selective due to greaseless, easily removable, emollient and transparency also used got delivery of analgesic Antiinflammatory, antifungal, antiacne and various cosmetic formulation. Mefenamic acid 2-[(2,3-dimethylphenyl)amino]benzoic acid, it is a non-steroidal anti-inflammatory agent . Due to Oral administration this drug may produce severe gastrointestinal side effects like-ulceration and gastro intestinal bleeding. To overcome this of this problem lies in the fact that, topically applied NSAIDs are safer than oral NSAIDs.The purpose of the study is to prepare an emulgel of Mefenamic Acid using different gelling agents. After preparation of emulsion it get incorporated in different gelling agents like Carbopol 940, Carbopol 934, Lutrol 127 and Lutrol 87. After completion it's formulation evaluation of Mefenamic Acid emulgel carried out for Physical appearance, Spreadability, Extrudability, Rheological studies, Drug content and in vitro release, ph. [1, 3,23]

KEYWORDS:

Emulgel, tropical drug delivery, hydrophobic drug, Mefenamic acid, emulsifying agent,

INTRODUCTION:

Topical drug delivery system is a system in which direct application of a formulation containing an active pharmaceutical ingredient to the skin to obtain the localizing effect of drug.Topical drug delivery system has the ability to deliver drug more selectively to a specific site and prevention of incompatibility associated with gastro-intestinal.Also topical deliveries by avoiding first pass metabolism provide an increased bioavailability and consistent delivery for an extended period.In topical drug delivery system, drug reaches to the site of action via diffuses out of the delivery system and their absorption takes place. These are applied to the healthy or diseased skin as a wide range

of preparations in both aesthetic and dermatological cases. The formulations come in a variety of forms, ranging from solid to semisolid to liquid. Drugs applied topically on application site or for have systemic effects. absorption of drug through the skin is improved when the drug substance is in solution which has a favourable lipid/water partition coefficient.Dissolution and diffusion of the drug in the delivery of hydrophobic medications, and permeation through the stratum corneum in the administration of hydrophilic pharmaceuticals, are the major drawbacks of topical dosage forms. In emulgel formulation, both oil-in-water and water-in-oil emulsions are widely utilized as carriers to deliver both hydrophilic and hydrophobic medications to the skin. The combination of gels and emulsions are used in the dosage forms are referred as Emulgels. preparation is perform by mixing an oil-in-water type or water-in-oil type emulsion with a gelling agent. The oil-in-water system is used directly to entrap lipophilic drugs, where as hydrophilic drugs are encapsulated in the reverse water-in-oil system. Mefenamic acid 2-[(2,3-dimethylphenyl)amino]benzoic acid is anon-steroidal anti-inflammatory agent with analgesic, anti-inflammatory, and antipyretic properties in response to therapeutic efficacy few toxicity issues are observed with inadequate reactivity that limits it's affinity oral administration of mefanamic acid respond serious toxicity as compare to subcutaneous and intramuscular. With respect to mode of action and toxicity similar to NSAIDS mefenamic acid which is class of fenamet, nevertheless posses unique property due to which topical application of NSAIDS like mefenamic acid is superior than oral[1][2]

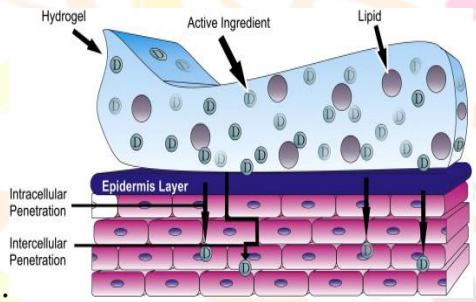

Fig:- Structure of emulgel[24]

TYPES OF EMULGEL :

1) Macroemulgel: these are opaque and commonly used emulgel with particle size of droplet of emulsion less than 400 nm which can easily observed under microscope. Ex-mefenamic acid emulgel prepared by using carbopol 940asgelling agent, liquid parrafin as oil phase, as penetration enhancer clove oil and mentha oil, further evaluated for rheological studies, spreading coefficient studies and invitro and skin irritation.

2) Nanoemulgel: it is combination of nanoemulsion and gel in which nanoemulsion is transparent, thermodynamicaly stable dispersion of o/w which stabilise by interfacial film of surfactant having particle size less than 100 nm. Ex- Carvidiolol nanoemulgel using oleic acid and isopropyl Myristate as oil phase and as surfactant tween 20 and carbitol and also carbopol 934 as gelling agent.

3) Microemulgel: these are transparent and thermodynamicaly stable type of emulgel with particle size of droplet is 10 to 100 nm the ingredients of microemulgel helps in penetration and absorption Ex-clotrimazole microemulsion by using capryol 90 as oil phase and as surfactant cremophore EL, carbopol ETD as gelling agent. [3]

CONSTITUENT OF EMULGEL

1) Aqueous phase_ water and alcohol is used to prepare emulsion base on aquos phase

e Ex- water and alcohol

2) Oil phase_ The oily phase of the emulsion is formed by the components like Mineral oils, either alone or in combination with soft or hard paraffins as the drug's vehicle as well as for their occlusive and sensory properties in topically administered emulsions. Nonbiodegradable mineral and castor oils, which have a local laxative action, are commonly used in oral preparations, as are fish liver oils or various fixed vegetable oils.

Ex_ cottonseed, archise

3) Emulsifiers_ Emulsifying agents used both to promote emulsification at the time of manufacture and to control the stability during a shelf life.

Ex-Polyoxyethylene sorbitan monooleate (Tween 80), Sodium stea, stearic acid , Polyethylene glycol 40 stearate.

4) Permeation enhancer_These are agents that interact with skin constituents to induce a temporary and reversible increase in skin permeability.

Ex- lacithin, urea eucalyptus oil, oleic acid, isopropyl myrist.

Permeability enhancer properties:

1) Penetration enhancers should act unidirectionally. That is, the therapeutic agent must be allowed to enter the body while preventing loss of endogenous substances from the body.

2) Penetration enhancers must be suitable for use in a variety of topical formulations and therefore compatible with both excipients and drugs.

3) Must be at an acceptable level in appearance.[2]

5) gelling agent_ These are the agents used to increase the consistency of dosage form as well as thickening agent.

Ex-Carbapol 934 , carbapol 940 ,HPMC

6) Humectant_ These are used to hydrate the skin.

Ex- glycerin, propylene glycol.

7) preservative _help to maintain its stability prolonged.

Ex-benzalkonium chloride, methyl paraben , propyl paraben.

8) Antioxidant_ Ex- BHA(Butylated hydroxy anisole) , BHT(butylated hyroxy Tolune), ascorbyl palmitate. [3]

IDEAL PROPERTY OF EMULGEL:-

- They should be nontoxic.
- They should be easily available.

 They should be cheap.

 They do not be contraindicated.

 They should chemically and physically be stable.[1]

FACTORS AFFECTING ON EMULGEL:

1) Physiological Factors-

1. Thickness of the skin
2. Ph of skin
3. Hair follicle density is the number of hair follicles in a given area.
4. Sweat gland density is a measure of how dense sweat glands are.
5. Lipidic content.
6. The flow of blood.
7. Hydration of skin.

2) Physiochemical Factors -

1.Partition coefficient.

2.Molecular weight less than400 Dalton.

3.Degree of ionization (only unionized drugs gets absorbed well).

4.Effect of vehicle[23]

Physiology of skin

majority of topical medicines are intended for use on the skin. For creating topical dose forms, a basic understanding of the skin and its physiological function is essential. The average adult body's skin covers about 2m2 of surface area. The non-viable epidermis receives nearly a third of the blood that circulates in the body. On the average, each square centimeter of human skin contains 40-70 hair follicles and 200-300 sweat ducts. Sweat and sebum-secreted fatty acids impact the pH of the skin's surface, which ranges from 4 to 5.6. There are four separate layers of tissue that make up the skin.[23]

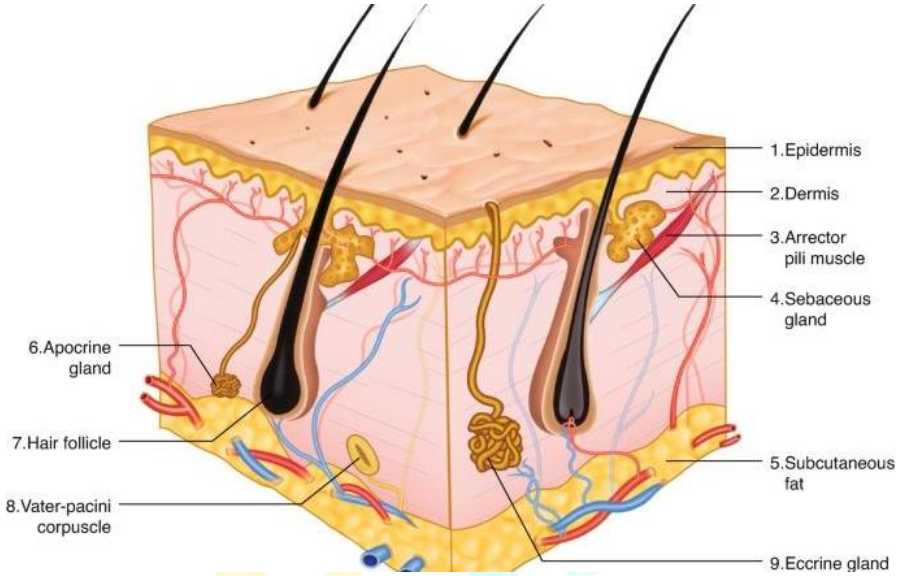

Fig: Structure of skin

MATERIAL RECQUIRD_

Mefenamic acid as sample from Flamingo pharmaceuticals Ltd. (Navi-Mumbai, India). Lutrol 127 and Lutrol 87 procured as gift sample from BASF (Navi-Mumbai, India). Carbopol 940, Carbopol 934, Propylene glycol, Tween 80, Methyl paraben, Propyl paraben, Dimethyl sulfoxide, Ethanol, Triethanolamine were obtained from S.D Fine Chemicals Ltd. (Mumbai, India). Span 80 was supplied by CDH Ltd. (Mumbai, India). Wintergreen oil was purchased from Siddhi aromatic. [23]

Preparation of mefenamic acid emulgel:

Gelling agents like Carbopol940, Carbopol934, Lutrol127 and Lutrol 87 are dispersed in the purifiedwater. pH should maintain at (6-6.5) by using TEA. The oil phase of the emulsion was prepared by dissolving Span 80 in light liquid paraffin and the aqueous phase prepared by dissolving Tween 80 in purified water. Methyl and Propyl paraben was dissolved in propylene glycol whereas drug MEFENAMIC ACID was dissolved in ethanol and dimethyl sulfoxide and both solutions were mixed with the aqueous phase. Both aquos phase and oily phase separately heated at 70 to 80 °c then oily phase is added continuously in aquos phase with continues stirring untill it get cooled at room temperature. With gentle stirring formed emulsion is mixed with gel at ratio of 1:1 proportion. [1][8]

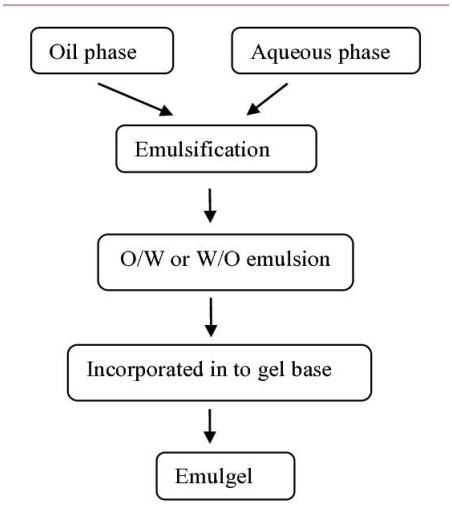

Fig : Chart of emulgel preparation[1]

EVALUATION:-

Emulgels were evaluated for their physical appearance,, Spreadability, ph, drug content, in vitro diffusion studies, extrudability, All studies were carried out in triplicate and average values were reported.

1) Appearance_

The appearance of the emulgel was visually checked for color, uniformity, concentration, presence of sand grains, and phase separation.

2) pH_ measurement

pH measurements are performed using a digital pH meter. The gel-like emulsion was stirred in distilled water until a homogeneous dispersion was formed and then left for 2 h. Use 1% solution of the prepared composition to bring the volume to 100 ml. pH measurements can be performed.

3) Spreadibility_

Spreadibility is adapted in lab for investigation the spreading ability . Spreadibility measurement is based on emulgel `slip' and `drag' qualities. It is built by wooden block if which at the base glass slid is fixed there is excess of emulgel is present under observation . Then emulgel is paced between this slide and next glass slide with the same size as fixed on ground state. 1 kg weight is placed on top of both slides for 5 minutes to release the air and provide consistent emulgel coating between slides. Then 80 gm pulled is applied to plates. The time required by top slides should cover and recorded the distance of 7.5 cm with the help of string tide to hook, the shorter the Interval the better will spreadibility.

Formula used to measure the spreadibility is ;

S = M. L / T

Where as,

S = spreadibility

M= weight tide to upper slide

L = length of glass slide

T = time taken to detach the slide[8]

4) Extrudability test:_

It is simplest test to determine how much force is required to extrude material from a tube.This method is used to evaluate emulgel formulations for extrudability. This study is based on the percentage of emulgel and emulgel extruded from a lacquered aluminum collapsible a 0.5 cm emulgel ribbon in 10 seconds. Extrudability improves when the quantity extruded increases. Each formulation's extrudability is measured three times and the average values are reported.

Extrudability= force required to extrude the material from tube[6]

5) Skin irritation test:-

This test is performed on either rabbit Or rat , in this formulation of 0.5gm if each is uniformly placed over 4 cm area on hairless skin .After 24, 48, and 72 hours of application of the formulation, the skin surface is examined for any kind of changes such as erythema redness(erythema) . [23]

6) drug content determination:-

1 gramme of emulgel is required for determination of content uniformity, It should be mixed in a suitable solvent to get a clear solution, filter it. Using a UV spectrophotometer, determine its absorbance. a standard drug plot is made in the same solvent,Using the same standard plot, the concentration and drug content can be determined by plugging the absorbance value into the standard plot equation.

7) invitro drug release study:-

It is carried out by using Franz diffusion cell, which helps to determine the drug release. Emulgel is evenly placed on the surface of the egg membrane. Between the donor and the diffusion cell's receptor chamber, the egg membrane is secured. To solubilize the medication, the receptor chamber is then filled with newly made solution ph(5.5), A magnetic stirrer is used to stir the receptor chamber. The 1.0 ml aliquots of the emulgels must be collected at appropriate time intervals, and the correctly diluted samples must then be analyzed for drug content using a UV visible spectrophotometer. Cumulative adjustments are used to determine the overall amount of medication released at each time period. It's function to calculate the total amount of medication released across the egg membrane. [4]

8) Dilution test:-

By introducing Continuous phase to a 50 to 100 times aqueous dilution of emulgel, phase separation and clearness were visually verified.

9) zeta potential:-

The zeta potential of the emulgel formulation is determined using the Zetasizer (Malvern Zetasizer). The result is computed when the formulation is placed in a transparent, disposable zeta cell. Cuvettes are soaked in methanol before being filled with the experiment's sample.

10) centrifugation study:-

This procedure is used to determine the emulgel's stability. After a week of preparation, it is completed. This experiment carried out in a minicentrifuge at 3000 rpm for 30 minutes.

ADVANTAGES:-

• Hydrophobic drugs easy to administered.

• Better loading capacity

• Improved stability

• Controlled release

• No intensive sonication

• Avoid first-pass dialogue.

• Prevention of gastrointestinal incompatibility.

• Take a more selective approach to specific sites.

• patient compliance improved with treatment regimens.

• Emulgel is convenient to use and easy to apply.[3]

DISADVANTAGES

• Skin irritation tends to dermatitis

• The possibility of allergic reactions

• The poor permeability of some drugs through the skin

• Drugs of large particle size are not easy to absorb through skin

• The occurrence of the bubble during formulation of emulgel [3]

PACKAGING OF EMULGELS :-

The emulsion is packaged in an aluminum tube with an internal coating of phenoxy-epoxy varnish and with a membrane seal closed with a propylene screw cap, or in a laminated aluminum tube closed with a cast seal.[1]

Marketed formulation:[23]

DRUG	PURPOSE	USES
Itraconazole	Formulation and evaluation of topical Itraconazole emulgel.	For the treatment of fungal infection.
Allopurinol	Design and development of allopurinol emulgel.	In the treatment of gout.
Ketoconazole	Formulation and evaluation of ketoconazole nanoemulgel	For the treatment of fungal infection.
Meloxicam	Formulation and characterization of Meloxicam loaded emulgel for topical application.	Anti-inflammatory
Ketoprofen	Formulation of in vitro and in vivo evaluation of microemulsion-based gel loaded with ketoprofen	Anti-inflammatory.
Oxiconazole	Formulation of Oxiconazole emulgel for topical drug delivery.	Fungal infection.

Summary:-

topical drug delivery system, a large number of formulations are used, but these formulation also have their own disadvantages. Major of these disadvantages can overcome by emulgel preparation. The emulgel preparation have proven that it is most convenient, better, and effective delivery system incorporation of emulsion into gel makes it suitable as a dual control release system to solve further problems such as phase separation, creaming associated with emulsion, and improvement of stability. preparation of emulgel is completed with three steps such as, preparation of emulsion, preparation of gel and incorporation of these two preparation. Such formulations always needs a proper evaluation. So here too, there are about 25 types of evaluation methods, including microscopic, flow, and rheological tests.[23]

COCLUSION:-

In the future, topical drug delivery will be widely used, which will improve patient compliance with treatment regimens. Emulgel is a new topical drug delivery method suitable for hydrophobic drugs. This is because it can also improve fluidity, adhesion, viscosity and extrudability. This will become a popular drug delivery system.

References:

1) K.P. Mohammade Haneef, Sherry Easo, P.V. Hafsa, Guru Prasad Mohanta, Chandini Nayar, 2013. Emulgel: An Advanced Review. Journal of Pharmaceutical Science and Research, 5(12), pp 254-258

2) Haedenia Anu, Jayronia Sonali and Jain Sanjay,2014. Emulgel: An emergent tool in topical drug delivery. A review International Journal of Pharmaceutical Science and Research, 5(5), pp 1653-1660

3) Kute S.B and Saudagar R.B. Emulsified Gel a Novel approach for delivery of hydrophobic drugs,2013. A review on emulgel. Journal of Advanced Pharmacy Education and Research, 3(4), pp 368-376

4) 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.

5) 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

6) 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.

7) Shah A. Arpan, kamdar Kamal, Shah Rushabh, Keraliya A. Rajesh., 2013. Emulgel: A Topical Prepartions for Hydrophobic Drugs. Ph Tech Med, 2(5), pp 370-376.

8) Bhatt Preeti, Gnanarajan. G, 2013. Emulgels: A Novel Formulation Approach for the Topical Delivery of Hydrophobic Drugs A Review. International Research Journal of Pharmacy, 4(2),

8) S application of topical drug delivery. Indian J. Pharm. Biol. Res.2017; 5(1):25-33.

9) Brijesh Mahesh Patel, AshwinBhanudasKuchekar and SaishRajendraPawar, Emulgel Approach hailendra Kumar Sah, AshutoshBadola, Bipin Kumar Nayak. Emulgel: magnifing the

10) to Formulation Development: A Review, BIOSCIENCES BIOTECHNOLOGY RESEARCH ASIA, September 2021. Vol. 18(3), p. 459-465

11) Parihar N, Saini M, Soni SL, Sharma V, Emulgel: A Topical Preparation,Asian Journal of Pharmaceutical Research and Development. 2020; 8(3):196-201.

12) K.P.MohammedHaneefa, Sherry Easo, P.V.Hafsa , Guru Prasad Mohanta , ChandiniNayar, Emulgel: An Advanced Review, Journal of Pharmaceutical science and Research, Vol.5(12), 2013, 254 – 258

13) VijayantaDhawas, DishaDhabarde and ShaktipalPatil .2020, Emulgel : A Comprehensive Review for Novel Topical Drug Delivery System. Int J Recent Sci Res. 11(04), pp. 38134-38138.

14) ShokriJ ,AzarmiSh, Fasihi Z, Hallaj-Nezhadi S, Nokhodchi A, Javadzadeh Y. Effects of various penetration enhancers on percutaneous absorption of piroxicam from emulgels. Res Pharm Sci 2012; 7(4):225- 234.

15) Ibrahim MM, Shehata TM. The enhancement of transdermal permeability of water soluble drug by niosome-emulgel combination. J Drug DelivSciTechnol 2012; 22(4):353-359

16) Nikumbh KV, Sevankar SG, Patil MP. Formulation development, in vitro and in vivo aluation of microemulsion-based gel loaded with ketoprofen. Drug delivery. 2015 May 19;22(4):509-15

17) Padmalatha K. Formulation And Evaluation Of Oxico. International journal of current research , 2017;9 (10):

18) Parihar N, Saini M, Soni SL, Sharma V, Emulgel: A Topical Preparation,Asian Journal of Pharmaceutical Research and Development. 2020; 8(3):196-201.

19) S. Gousia Begum*, C.MadhusudanChetty, Vijay Kumar Voleti, B.Pavithra, B.Akhila, C.Gayathri,S.Ruksar and T.Sravani, A Review on Emulgels-A Novel Approach for Topical Drug Delivery, Asian Journal of Pharmaceutical Research and Development. 2019; 7(2):70-77

20) Naga Sravan Kumar Varma V, Maheshwari PV, Navya M, Reddy SC, Shivakumar HG, Gowda DV. Calcipotriol delivery into the skin as emulgel for effective permeation. Saudi Pharm J 2014;22(6):591-599.58876-58878

21) https://doi.org/10.1016/j.jsps.2011.08.001

22) Review for Analytical Methods for the Determination of Mefenamic AcidT. V. Ashira1, T. Mohamed Rafeeque1, Saba Maanvizhi2 S. Kathirvel1 P. C. Indukala1 and S. Safeetha3

23) Abdelhadi Adam Salih Denei1Dr. M. Sunitha Reddy21,2Department of pharmaceutics, Centre for Pharmaceutical Sciences, Institute of Science and Technology, Jawaharlal Nehru Technological University Hyderabad, Kukatpally, Hyderabad, 500085, Telangana, India

24) https://doi.org/10.1016/j.jconrel.2013.06.030