Development and characteristics of topical gel containing nimesulide: A review

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Abstract

Topical drug delivery system are becoming more and more popular and thus multiple drug have been effectively administered for each local and systemic action a maximum of non-steroidal anti-inflammatory drugs (NSAIDs) in recent years to raise awareness of these drug to deliver drugs topical gel protect against gastrointestinal irritation overcome "first pass" effect and maximize their action since the gel is not sticky and require less strength throughout the composition it has a higher dosage than topical formulation when evaluating an ointment. Nimesulide is a common non-steroidal anti-inflammatory drug (NSAIDs) that is effective in relieving a wide range of pain and inflammations but is more tolerated than other NSAIDs the terminal half-life of nimesulide is about 4 hrs. it is Cox 2 inhibitor used for variety of inflammatory pain and fever state gel are cross linked polymer network that expand in a liquid medium it’s properties mainly depend on the interaction of solid polymer and liquid component the gel does not spread evenly gel formulation provide an appropriate these delivery system for the drugs are less greasy and can be easily removed from the skin.

Keywords: Anti-inflammatory; Nimesulide; Gastrointestinal; Topical gel; Polymer; Skin

1. Introduction

Topical drug delivery system is targeted drug delivery system the intact of skin and through the directly systemic circulation although a wide variety of semi-solid formulation predominant in local delivery system [1], foams spray cured powder solution and healing adhesive system are used we develop. Currently the most common form of drug administration is oral administration this is the important advantage of being easy to administer but it has serious drawback, especially because of its low bioavailability due to liver metabolism (first pass) and a tendency for blood level to raise sharply (both high and low) it can be high performing or often redundant and important to overcome these difficulties [2]. state of the art product an effective topical formulation should provide a chemically stable environment in dispenser suitable for receiving several different themselves have additional physical effects on the skin such as drying clogging, or moisturizing research and technology has led to a better understanding of the physics, chemistry, pharmacodynamics, pharmacokinetics, of drugs used to treat acne [3]. These discoveries have led to the development of the new delivery system and that can improve the efficiency tolerability and cosmetic acceptability of the topical formulation in addition to physical and chemical stability topical formulas must be aesthetically pleasing and may require a variety of additives the composition should ensure optimal penetration of the drug into complex skin tissue pH of skin is about 5.5 therefore the pH of the formulation may change after application to the skin [4].

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2. Drug profile

2.1. Nimesulide

Nimesulide is a second generation non-steroidal anti-inflammatory drug widely used for long-term treatment of rheumatoid arthritis and inflammation. The biological half-life is 3-4 hours. Oral nimesulide has been associated with side effects such as gastrointestinal upset, epigastric pain, nausea, heartburn, vomiting, and diarrhoea. Topical drug administration prevents these side effects and offers potential benefits for rectal drug delivery.

2.1.1. Molecular formula

Molecular formula: C12H12N2O5

2.1.2. Molecule weight

Molecule weight: 308.31

2.1.3. Chemical structure

2.2. Advantage of TDDS

- Avoid gastrointestinal incompatibilities
- Avoid first pass metabolism effects
- Avoid fluctuating drug level
- Self-administration possible
- Increase effective of treatment
- Maintain effective plasma drug concentration

2.3. Disadvantage of TDDS

- Due to the natural limitations of drug supply due to skin in-permeability only relatively potent drugs are good aspirant for TDDS.
- Some patients develop contact dermatitis at the site of application of one or more systemic component that requires demobilization.
- The barrier function of the skin varies from place to place from person to person and from age to age.
- Clinical need is another area that need to carefully examined before deciding to develop a transdermal product [5].

2.4. Anatomy of skin

The skin is the complex organ that covering the entire surface of the body it provide a physical protective barrier between the body it provide and the environment prevent the loss of water and electrolytes, reduces the penetration of chemicals and protects against pathogens microorganism the skin is important for thermoregulation and is used for immunological monitoring it contains sensory and autonomic nerves as well as sensory receptors that sense incoming stimuli such as touch vibration pressure, temperature, pain, and itching.
Skin is an important aspect of appearance and is the primary focus of many surgical and non-surgical skin procedures. Chronological skin changes or skin changes associated with photo aging such as wrinkles, laxity, and pigmentation encourage patients to undergo cosmetic procedures to improve the appearance of their skin [6].

2.5. layer of skin

2.5.1. Epidermis

The epidermis is the most superficial layer of the skin and consists of keratinized stratified squamous epithelial which varies in thickness in different parts of the body. The palms and soles of the feet are the thickest there are no blood vessel or nerve endings in the epidermis but the deeper layer penetrates the interstitial fluid of the dermis providing oxygen and nutrients and draining the asymptotes epidermis are the several layer of the cell and that prolong from the deep of the embryonic layer and to the superficial stratum corneum superficial cells are flat, thin nuclear free dead cells or squamous cells in which the cytoplasm is replaced by protein keratin these cells are constantly being erased and replaced by cells originating from the cotyledon and gradually migrate to the surface it takes about 40 days to completely replace the epidermis. Hair sebum and sweat ducts pass through the epidermis and reach the surface. The surface of epidermis protrudes from the cellular projection of the dermis called papillae. The pattern of bridges very from person to person and the impression they give a fingerprint. The downward protrusion of the germ layer between the papillae is believed to support the nutrition of the epidermal cells and stabilize the two layers to prevent shear damage. Acute trauma causes dermis and epidermis to separate and accumulation of serous fluid leads to blistering.

Classification of epidermis

- Stratum lucidum
- Stratum granulosum
- Stratum spinosum
- Stratum basale

2.5.2. Dermis

The dermis is Finn and elastic it consist of matrix containing connective tissue and collagen fibers woven into elastic fibre breaks occur when the skin is overstretched resulting in permanent stretch marks and obesity. Collagen fibers bind to water giving the skin tension but as this ability decrease with age, wrinkles appear. Fibroblasts, macrophages, and mast cells are the most important cells in the dermis. At the base of the innermost layer is the areola and varying amount of adipose tissue (fat).

- Dermis are divided into some structure
- Blood vessel
- Lymph vessel
- Sensory (somatic) nerve ending
- Sweat gland and their ducts
- Hairs Arrector Pilli muscles and sebaceous gland

2.5.3. Hypodermic or subcutaneous tissue

The hypodermic or subcutaneous tissue support the epidermis and dermis acts as store and fat and this layer helps regulate temperature provide nutritional support and mechanical protection transports major blood vessel and nerves to the skin and contains the senses you can transdermal drugs and drugs must pass through three layers to reach the systemic circulation.

2.6. Gels

gels are transparent opaque containing semisolid dosage form with containing one or more active ingredient with in containing both solid as well as liquid component with three dimensional structure gels are faster release to the other dosage form as compared to ointment and cream.

USP gel are the semisolid formulations containing a suspension of small inorganic particle or large organic molecule that permeate into liquid transdermal gels have different properties fat free thixotropy easy to remove discolored and proportional to the amount of excipients [7].
2.6.1. Properties of gel

- Ideally the gelling agent should be inert and safe for pharmaceutical or cosmetic use and should not react with other in gradients in the composition.
- The gelling agent contained in the formulation must from a sufficient amount of solid during storage which can easily destroyed by the shear forces generated by shaking the bottle squeezing the tube or topical application.
- Appropriate antimicrobial agent must be present to prevent microbial attack
- The eye gel must be sterile
- topical gel should not be sticky

2.6.2. Ideal characteristic of gels

Swelling

The gelling agent used to create the gel may swell on contact with a liquid medium the swelling of the gel is dependent on the gelling and indicates the strength and adhesion of the particles within the gel.

Synergetic

Most of the gel dissolve or release water or liquid during their stay and the release of liquid from gel after several days of storage is called syneresis there gel show that non adequate amount of gelling agent reduce and it also shows that the formulation is the thermodynamically unstable and gel are syneresis free.

Structure

The hardness of gel is mainly depending on the gelling agent and the selection of gelling agent are the most important in the formulation and gelling agent are responsible for binding the viscosity (resistance to flow) binding between particle and medium are the used in the formulation [8].

2.6.3. pH

the pH of the gel must be isotonic fluctuations in the pH of the gel can irritate the skin.

2.6.4. Spreadability

The gel strength will be very good indicates the area covered with gel.

2.6.5. Classification of gel

On the basis of nature of colloidal phase
- Inorganic gel (two phase system)
- Organic gel (one phase system)

On the basis of nature of solvent
- Hydrogel (Aqueous gel)
- Xerogel
- Organic gel (Non Aqueous gel)

On the basis of rheological properties
- Plastic gel
- Pseudo plastic gel
- Thixotropic gel

On the basis of physical nature
- Elastic gel
- Rigid gel
2.7. Formulation Design [9,10]

2.7.1. Polymer

Natural
collagen gelatin

Polysaccharides
Alginic acid, Agar, Tragacanth, Gaur Gum, Pectin, Xanthin

Semi synthetic polymer
Cellular derivative: Hydroxy ethyl cellulose, methyl cellulose, carboxylic methyl cellulose, Hydroxy propyl cellulose,

Synthetic polymer
carbopol 934, carbopol 941, carbopol 940, Poloxamer, polyvinyl alcohol, polyacrylamide, polyethylene,

2.7.2. Inorganic substance
Bentonite, Aluminum hydroxide,

2.7.3. Surfactant
Brij 96, cetostearyl alcohol.

2.7.4. Additives used in gel formulation
Preservative
methyl paraben, propyl paraben.

Drug solubilizer
Triethyl - o - amine, pvp (polyvinyl pyrolidine)

Stabilizer
EDTA

2.8. Evaluation of gels [11, 12, 13]

2.8.1. Melting point Determination
Determination of melting point of the gel was open capillary tube method.

2.8.2. Physical appearance
the prepared gel formulation is checked for the visually pH, color, homogeneity, consistency, grittiness and phase separation.

2.8.3. Determination of pH
the pH values of the aqueous solution nimesulide gel were measured by the Digital pH meter.

2.8.4. Viscosity measurement
The viscosity of different nimesulide gel formulation was determined at the Brookfield viscometer.

2.8.5. Spreadability
To the determined the spreadability of the gel was evaluated by the using the slide method 1gm of gel are placed between the two slides and the pre weighted plate was kept above the gel and the more weights are added on the plate
and until the gel is spreading stop and the final cumulative weight and the total time taken by the gel spread was measured and noted. Then the total weight applied and the mass of the gel were compared by the time.

\[ S = \frac{M \times L}{T} \]

2.8.6. Drug content studies

Accurately weight 1 gm of gel to a 100 ml volumetric flask, make up to 100 ml with phosphate buffer (pH 7.4), pipette to 1 ml, dilute to 10 ml after dilution and measure the absorbance using a Shimadzu 1700 UV 396 visible light spectrophotometer nm.

2.8.7. In vitro diffusion study

In vitro diffusion studies were per-diffusion cells. (1 g) of gel was evenly applied to the dialysis membrane surface, and the dialysis membrane is clamped between the donor and the receptor compartment and the diffusing cell are filled with the phosphate buffer pH 7.4. and receptor chamber was the stirred by the magnetic stirrer. The studies carried out at 37 ± 0.5 °C and 100 rpm and the samples were withdrawn from the sampling port of the reservoir compartment at the regular interval and absorbance was measured by using the Shimadzu 1700 UV visible spectrophotometer at the 396.5 nm.

2.8.8. Extrudability

The tests were carried out using a Pfizer hardness tester. Filled 15 g of gel into a collapsible aluminum tube, and the plunger was the adjusted and the hold tube and the properly the pressure of 1 kg/cm2 was the applied for the 30 sec and the procedure was repeated at three equidistance places of the tube and the test carried out in triplets.

2.8.9. Skin irritation test

The hairs of the dorsal side Wister of the albino rats was removed of the clipping one day before the experiment and rabbit are divided into 3 groups the group served as the control group 2. received the optimized formulation of the group 3. received 0.8 v/v of the aqueous solution of the formalin as a standard irritant as finally the application sites were the graded to the visual of scoring score.

2.8.10. Stability studies

The optimized the formulation of the F4 was the subject to the stability testing for the period of three months as per of the 8 ich norms and at the temperature of 25 ± 20°C and with the relative humidity RH = 60±5% and 400 ± 20°C with the relative humidity RH =75±5% the optimized formulation of F4 was analyzed for the in appearance and pH and the percentage of the drug content and the in vitro diffusion stud.

2.8.11. Drug release studies

The models are tested for explain the kinetics of the drug release to the analyse to the mechanism of drug release rate for the kinetics of the formulation and its obtained the data was fitted into the zero order first order Higuchi and Korsmeyer Peppa’s release model of the study the drug release from the formulation.

3. Conclusion

Nimesulide is a common non-steroidal anti-inflammatory drug effective in relieving pain and inflammations. It is more tolerated than other NSAIDs the terminal half-life of nimesulide is about 4 hrs. It is Cox 2 inhibitor used for variety of inflammatory pain and fever state gel are cross linked polymer network that expand in a liquid medium it’s properties mainly depend on the interaction of solid polymer and liquid component the gel does not spread evenly gel formulation provide an appropriate these delivery systems for the drugs are less greasy and can be easily removed from the skin [14, 15].
Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

References


