International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 693-699 www.ijprajournal.com ISSN: 2249-7781

A Comprehensive Review on Topical Gel

Vaibhavi Vijay Autade*, Suvarna Jagannath Shelke
Department of Pharmaceutics, S.M.B.T. College of Pharmacy,Dhamangaon, Nashik, M.S. India-422403
**Address for Correspondence: Department of Pharmaceutics, S.M.B.T. College of Pharmacy, Nashik, M.S., India-422403*

Submitted: 25-03-2024 Accepted: 05-04-2024

ABSTRACT
Topical gels are semi-solid formulation in which a liquid phase is encapsulated within three-dimensional polymeric matrix consisting of either synthetic or natural gum. Compared to other dosing forms, topical gels are safer and more efficient. In a liquid media, a cross-linked polymer network expands to form a gel. Topical formulations offer both local and systemic effects, which are often applied to the skin.Based on their physical makeup, rheological characteristics, colloidal system, and solvent system, gels are categorized. Topical gel formulations distribute drugs more effectively since they are quicker to remove from the skin and less oily. The property of topical gel formulations are less oily and more readily removable derived from the skin renders them an excellent choice for drug delivery. Better gel formulation is available.

Key words: Synthetic gum , Skin , Drug administration

I. INTRODUCTION

Topical gels are uniform semi-solid, formulations employed for the prevention and treatment of skin ailments.[6] Many of these ailments that afflict man are now treatable, preventable, and eradicable thanks to research. Due to its advantages over cream and ointment,Topical gels are a common dosage form used in cosmetics and skin conditions treatments for the delivery of topical medications. They may be divided into organogels and hydrogels because These gels are formulated through the combination of gelators, solvents, active ingredients, and supplementary excipients. The characteristics of the gelators, solvents, drugs, and excipients employed in drug preparation and formulation are dependent on each other. Topical formulations are used to acheievelocalized results at the application location, primarily because the drug penetrates into the subcutaneous layer of the skin or mucous membrane. Due to the hydrophilic nature of gels, the medicine or active component was released quickly. A gel is made up of two components that are three-dimensionally cross-linked and include a sufficient proportion of liquid medium to create an appropriate stiff network that immobilizes the fluid continuous phase.[14,15]

The classification of gels by the United States Pharmacopeia (U.S.P.) involves identifying them as semi-solid structures consisting of a dispersion of either small inorganic particles or large organic molecules, which are enclosed and mixed within a liquid medium. Gels exhibit a dual-phase system where inorganic particles are evenly dispersed rather than dissolved in the continuous phase, while significant organic molecules dissolve in the continuous phase, creating flexible, randomly coiled chains. The nature of bonding greatly influences the properties of the gel.

Gels can be either irreversible or reversible .Reversible gel often have hydrogen bonds whereas irreversible gel typically have covalent bonds. Excessive angiogenesis in tumor cells results in the presence of significantly big gaps in the vascular walls.

The aim of this study is to perform a comprehensive assessment of gel-based treatments for skin cancer therapy, while also discussing significant drawbacks and potential advancements in gel formulation. A concise overview of commonly used excipients and their functions is provided, alongside prevalent techniques for characterization. The paper presents documented methodologies for utilizing gels in topical chemotherapy administration.

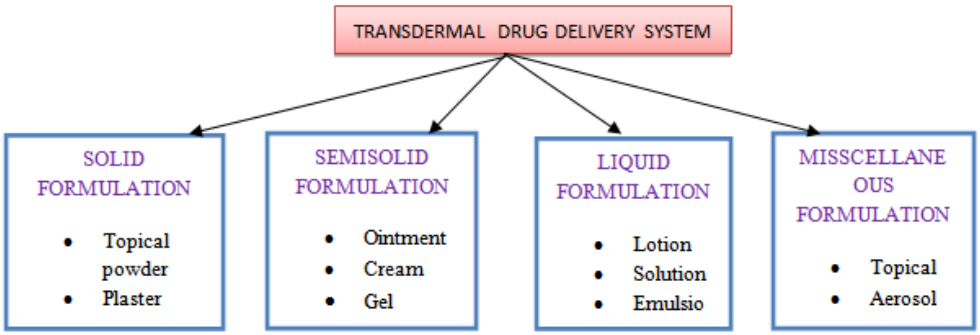
Topical Drug Delivery System

To address skin conditions such as eczema, topical drug delivery (TDD) is a method of administering medication that allows the application of the topical formulation onto the skin. Topical medication formulations encompass corticosteroids, antibiotics, antiseptics, and antifungals. A skin conveyance framework can be characterized as the substance that conveys a specific kind of prescription drugs into contact with andtransdermally. The test for skin

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 693-699 www.ijprajournal.com ISSN: 2249-7781

drugsconveyance is the vehicle across the skin boundary.

Table no.01"Categorization of Topical Drug Delivery System"



ADVANTAGES OF TOPICAL DRUG DELIVERY

1) Minimized First-passmetabolism: Topical treatment can avoid the first pass liver metabolism that may be experience by orally delivered pharmaceuticals, improving their bioavailability and effectiveness.
2) Avoidance of gastro intestinal incompatiability .
3) Reduce Systemic Side Effect: Topical medications when applied directly to skin or mucous membrane. Typically pose a reduce risk of inducing systemic side effect in a contrast to medication administered orally or intravenously.
4) Cosmetic Advantages : Some topical formulations may provide aesthetic advantages, such as enhancing skin appearance or hastening the healing of wounds.

DISADVANTAGES OF TOPICAL DRUG DELIVERY

1) Inadequate skin permeability is a challenge for certain drugs.
2) Drugs with larger particle sizes face barriers to skin absorption.
3) Medications necessitating high blood concentration levels pose limitations for administration through the skin.
4) Barrier function changes from person to person and within same person.
5) Possibility of allergic reactions.

ANATOMY OF SKIN

The skin, encompassing the entire body, acts as a vital shield, safeguarding against heat, light, injuries, and illnesses.The three interdependent tissues form the bulk of human skin. "Epidermis" refers to the stratified, cellular, and vascular layer.

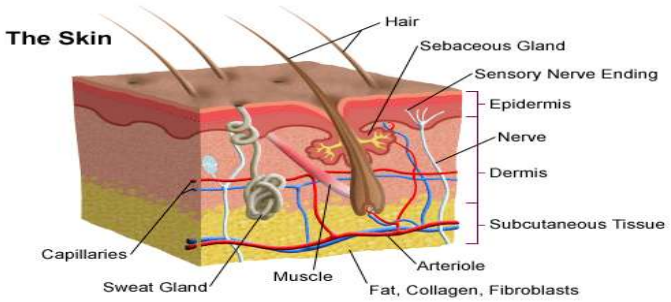


Fig 1: The Skin

"The skin comprises three distinct layers, each with specific functions:"
1] The Epidermis
2] The Dermis
3] The Subcutaneous Fat Layer (Hypodermis)"

1) Epidermis: The epidermis consists of five layers , namely :

a) Outermost layer
b) Transparent layer
c) Grainy layer
d) Spiny layer
e) Basal layer

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 693-699 www.ijprajournal.com ISSN: 2249-7781

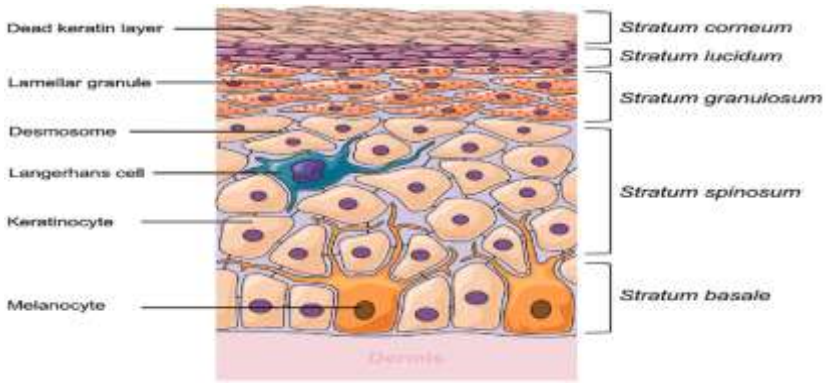


Fig 2 : Epidermis

The epidermis, situated at the skin's surface, does not possess a direct blood supply for nourishment.

2)Dermis

The dermis, located within the middle layer of the skin, consists of the following elements:

- Blood vessels
- Lymphatic vessels
- Hair follicles
- Sweat glands
- Collagen fibers
- Fibroblasts
- Nerve endings
- Sebaceous gland

The skin measures a thickness of 3 to 5 millimeters. It plays a significant part in controlling temperature as well. There are nerves that cause pressure and discomfort to be felt. The sensitive area, sweat organ, oil organ, hair follicles, and blood vessels make up the dermis.

3) Hypodermis

The hypodermis, also known as the subcutaneous layer, resides beneath the skin and acts as the interface between the skin and underlying body tissues, including muscles and bones. This subcutaneous tissue performs various functions such as supporting the epidermis and dermis, functioning as a fat storage site, aiding in temperature regulation, providing nourishment, offering mechanical protection, facilitating the transportation of main nerves and blood vessels that supply the skin, and housing sensory organs that allow for the systemic movement of transdermal drugs. It's a crucial site for fat storage, acts as a connecting layer between bones and muscles, and plays a role in insulation, protection, and temperature regulation. The hypodermis is a complex system made up of several glands, tissues, cells, and blood arteries that cooperate to safeguard the body and make sure it functions appropriately.

STRUCTURE OF GEL

A gel consists of either synthetic or natural polymers, forming a 3D structure within a dispersion medium. The specific connections formed and the particles involved impact the gel's structure and properties.Upon application, the liquid evaporates, entrapping the medication within a fine layer of the gel matrix that coats the skin. The type of bonding and particle characteristics influence the gel's structure and properties. A gelator is introduced into a mixture of solvent and active ingredients to create pharmaceutical gels. Topical gels serve as a medium for the application or transport of active medications through the skin. The 3D mesh of the gel holds the active drug molecules, which are then delivered to the intended site of action. USP gels are semi-solid formulations comprising large organic molecules or small inorganic particles that penetrate into liquid transdermal gels. These gels exhibit fat-free thixotropy, are easily removable, and their coloration is inversely proportional to the amount of excipients used.

Characteristics of gel

Gels differ from other dosage forms in that they have specific characteristics related to swelling, synergism ageing, stiffness, and the rheology.

a) Structure

Selecting the appropriate gelling agent is a critical aspect of formulation because it influences the gel's hardness and plays a role in binding viscosity between particles and the medium .

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 693-699 www.ijprajournal.com ISSN: 2249-7781

b) Swelling

Swelling occurs when the gelling agent gets into touch with the liquid and begins to absorb water, increasing the volume.

c) Aging

Aging refers to the process of aggregation that occurs more slowly in colloidal systems. Consequently,a more concentrated network of the gelling agent gradually develops.

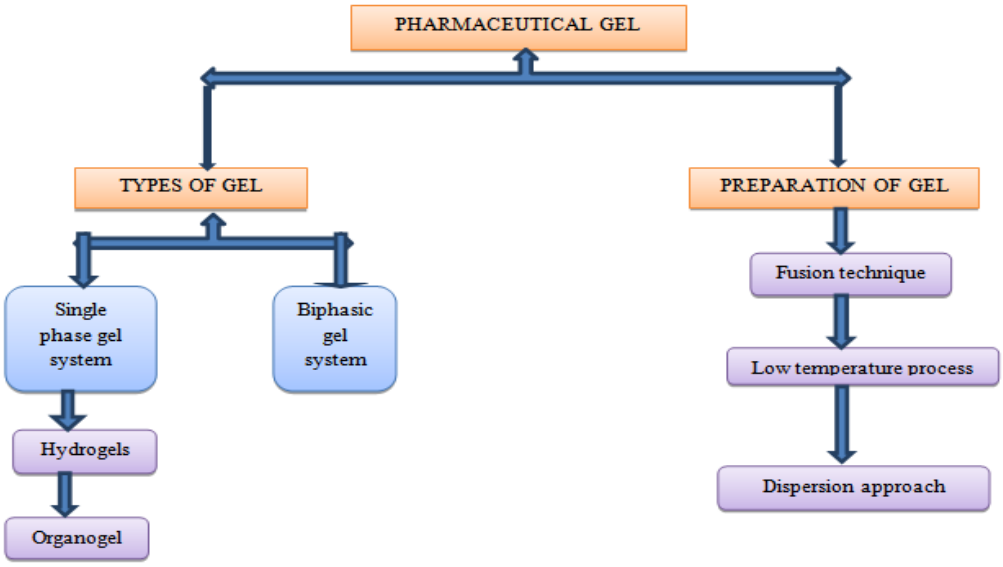
d) Syneresis

Numerous gel structures become compressed after standing. At the top layer of the gel, the interstitial fluid congregates and interacts. Along with natural hydrogels, organogels and inorganic hydrogels have also demonstrated this syneresis cycle. As the polymer cluster grows, syneresis frequently intensifies smaller

e) Rheology

Flocculated strong dispersion and gelling speciality arrangements are two instances of faux flexibility. Showing a reduction variation in thickness and an elevation in shear stress characterize non – Newtonian float conduct. A tighter organization of the gelling specialized eventually forms as n gels grow, upending the questionable design of inorganic trash diluted in water.

Table 2



Preparation techniques :

There are three steps of method of preparation they are as follows :

i. Fusion method
ii. Cold method
iii. Dispersion method

Depending on the size of the preparation, two primary methods are employed to produce semisolid dosage forms. One approach involves creating the medication at elevated temperatures by blending liquid or liquefied components and dispersing solids. Alternatively, the medication can be incorporated into an already-prepared semisolid base (cold incorporation). Cold incorporation is utilized when adding smedication to a preexisting semisolid base or when the vehicle is sensitive to heat, such as plastibase.

1) Fusion Method: This technique includes heating the ingredients to a high temperature and combining them together until a semi-firm texture is obtained.

2) Cold technique: With the exception of any drug or active pharmaceutical ingredient, all substances in this procedure are components, which are simultaneously heated and combined. The mixture's temperature is then decreased, the medicine is added, and until the gel hasn't formed, more ingredients are added and the blending process is repeated.

3) Dispersion Method: In this method, the gelling agent is combined with water until it starts to

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 693-699 www.ijprajournal.com ISSN: 2249-7781

expand. Subsequently, the drug is incorporated and dissolved in the medium if necessary. If adjustment of the gel's pH is required, a buffer solution can be added.

FORMULATION OF TOPICAL GEL

Balancing the proportions of polymer and solvent is essential for creating a gel. The gelling point, often referred to as the critical concentration, marks the threshold at which the gel forms, causing a significant increase in viscosity. Factors such as the hydrophilic-lipophilic balance of the components, interactions between the polymer and solvent, structural uniformity, polymer molecular weight, and the flexibility of the polymer chain can collectively influence the determination of the gelling point. Direct proportionality exists between the gelling point and the degree of elasticity. Solvents with different affinities for that polymer can change the gelling point's value. [22-24]

- **Antioxidant** - These are utilized to increase the therapeutic compounds chemical stability as they are susceptible to oxidative destruction. Typically, while creating medicinal gel, water-soluble antioxidants are used. For instance, sodium formaldehyde and sodium metabisulphite.
- **Preservatives** - Pharmaceutical gel is preserved throughout formulation to stop microbial growth or unfavorable chemical changes from causing degradation. For instance, phenolics, methyl paraben, and propyl paraben. [12]

As per the European Pharmacopoeia, gels are categorized as semisolid preparations for topical use, composed of appropriately gelled liquids. The formation of a gel involves achieving a harmony between the solvent and polymer.The gelling point, also referred to as the critical concentration, signifies the threshold at which viscosity notably increases.

Forcertain gels, temperature manipulation is necessary, such as heating the liquid, thoroughly incorporating the polymer, and allowing it to cool for proper setting. Conversely, some gels should not be heated, as elevated temperatures can disrupt critical bonds, like hydrogen bonds.[20,21]

Key factors influencing the formulation of topical gels encompass aspects like color,fragrance,spreadability,extrudability,viscosity ,pH,texture,susceptibilityto microbiological contamination, and bioavailability .The constituents of the vehicle should facilitate enhanced skin penetration for the medication.The design of the formulation significantly influences the characteristics of the gel, including its consistency and viscosity. In order to ensure effective medication delivery and proper adhesion and retention at the application site, consistency and viscosity are crucial factors for gels.The gelator , solvent, medication, and excipients are four major categories that may be used to group the constituents in topical gel formulations.

EVALUATION OF TOPICAL GEL

1) Appearance and Homogeneity
2) pH of gel
3) Grittiness
4) Skin irritation study
5) Spreadability
6) Viscosity[17,18]

1) Appearance and homogeneity: Visual inspection was used to gauge one's physical characteristics and uniformity. The produced gels were all visually examined for homogeneity after being put in thecontainer. They underwent inspections to go over them and look for aggregates.checked the gels that had been made for color, clarity, texture, transparency, and any grit.[16]

2) pH of gel:A digital pH meter was employed to measure the pH of gel following the dissolution of 1 gram of the gel into the medium.

3) Grittiness: The existence of particles in all the formulations was examined under a light microscope, but no discernible particulate matter was found. So, of course, the gel condition of independence requires preparation. Specific subject and free of gritty elements, as required for any topical planning.[12]

4)Skin irritation study : Skin irritation testing is conducted on guinea pigs weighing between 400-500 grams, irrespective of gender. These animals are provided with standard animal feed and have unlimited access to water while being housed in typical conditions. A 4 cm^2 area of the guinea pigs' back hair is shaved, with one side designated as the control and the other as the test area. Gel (500 mg per guinea pig) is applied twice daily for a period of 7 days. After this period, the application site is examined for any signs of sensitivity, and any reactions are categorized on a scale of 0 to 3 based on their severity, ranging from no reaction to severe erythema with or without edema.

5)Spreadability: When the gel is administered to the skin or another impacted region, it rapidly covers the entire visible area on the surface. The effectiveness of a specific aspect is also determined

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 693-699 www.ijprajournal.com ISSN: 2249-7781

by its level of recognition. The spreadability is gauged by the time it takes for two slides to part ways when compressed with the gel in between, under a designated stress. Enhancing spreadability is achieved by dividing two slides into smaller sections in a shorter duration.

Spreadability is calculated by using formula :

S = M . L /T
Where ,
M= wt.tied to upper slide
L= length of glass slide
T = time taken to separate the slide.

6)Viscosity: To evaluate the viscosity of a formulated gel, employ a Brookfield digital viscometer. The gel is rotated at speeds of 0.3, 0.6, and 1.5 revolutions per minute, and the corresponding dial readings are noted for each speed. Viscosity is determined by multiplying the dial reading by a factor specified in the viscometer catalogs..

MARKETED PRODUCT LIST

Sr no	Drugs		Market product	Manufacturer
1.	Diclofenac diethyl ammonium		Voltaren Emulgel	Novartis Pharma
2.	Miconazole Nitrate,Hydrocortisone		Miconaz H emulgel	Medicalunion Pharmaceuticals
3.	Clindamycin , Adapalene		Excex Gel	Zee Laboratories
4.	Benzoyl Peroxide		Pernox Gel	Cosme Remedies Ltd.
5.	Metronidazole , Clindamycin		Lupigyl Gel	Lupin Pharma
6.	Clindamycin Phosphate, Allantion		Clinagel	Stiefel Pharma
7.	Diclofenac Sodium		Pennsaid	Nuvo Pharma
8.	Nadifloxacin		Nadicin Cream	Psyco Remedies
9.	Tezarotene		Zorotene Gel	Elder Pharmaceuticals
10.	Aceclofenac		Acent gel	Intra Labs India Pvt.Ltd.
11.	Clobetasol Propionate		Topinate Gel	Systopic Pharma
12.	Kojic Acid, DipalmitateArbutin		Kojivit gel	Micro Gratia Pharma
13.	Clotrimazole,Beclomethasone		Cloben Gel	Indoco Remedies
14.	Hibiscus,Liquorice and Natural Extracts		Levorag Emulgel	THD Ltd.

II. CONCLUSION:

Currently, an increasing number of individuals are turning to pharmaceutical gels due to their enhanced stability and controlled release attributes, surpassing other semisolid dosage forms. With superior skin absorption, topical gels heighten bioavailability. Opting for topical administration holds the primary advantage of circumventing first-pass metabolism, alongside exceptional patient compliance. When bioavailability is limited, topical distribution typically takes precedence over alternative medication administration routes. Clinical data underscores the safety and efficacy of topical gels as a viable treatment option for addressing skin-related ailments.

REFERENCES –

[1]. Bhushan Rajendra Patil, Anup Mukund Akarte, Pankaj Motilal Chaudhari, Kalpesh Shamkant Wagh, & Prakash Hiraman Patil. (2021). Development and characteristics of topical gel containing nimesulide: A review. GSC Biological and Pharmaceutical Sciences, 15(3), 295–301. https://doi.org/10.30574/gscbps.2021.15.3.0176

[2]. Samundre, P., Dangi, S., Patidar, T., & Maroti Shende, S. (2020). A REVIEW ON TOPICAL GEL (Vol. 8). www.ijcrt.org

[3]. Slavkova, M., Tzankov, B., Popova, T., & Voycheva, C. (2023). Gel Formulations for Topical Treatment of Skin Cancer: A Review. In Gels (Vol. 9, Issue 5). MDPI. https://doi.org/10.3390/gels9050352

[4]. Tarun Guleri, K., & Loveleen Preet, K. (2011). FORMULATION AND EVALUATION OF TOPICAL GEL OF ACECLOFENAC.Journal of Drug

Delivery & Therapeutics, 2013(3), 51. http://jddtonline.info

[5]. Sharma, U., Arjariya, S., Chouksey, R., & Sharma, N. (2022). A Review: Formulation and Evaluation of Pharmaceutical Gel. Journal of Pharmaceutical Negative Results, 13, 1344–1362. https://doi.org/10.47750/pnr.2022.13.S01.160

[6]. Samundre, P., Dangi, S., Patidar, T., & Maroti Shende, S. (2020). A REVIEW ON TOPICAL GEL (Vol. 8). www.ijcrt.org

[7]. Ayesha Ahmed un Nabi, S., Ali Sheraz, M., Ahmed, S., Mustaan, N., & Ahmad, I. (2016). Pharmaceutical Gels: A Review. In RADS-JPPS (Vol. 4, Issue 1).

[8]. Bhuyan, C., Saha, D., & Rabha, B. (2021). A Brief Review on Topical Gels as Drug Delivery System. Journal of Pharmaceutical Research International, 344–357. https://doi.org/10.9734/jpri/2021/v33i47a33020

[9]. Ayesha Ahmed un Nabi, S., Ali Sheraz, M., Ahmed, S., Mustaan, N., & Ahmad, I. (2016). Pharmaceutical Gels: A Review. In RADS-JPPS (Vol. 4, Issue 1).

[10]. https://en.wikipedia.org/wiki/Topical_gels

[11]. LovleenPreetKaur , Rajeev Garg,GD Gupta , a review on topical gel volume -3, 2010

[12]. Bhuyan, C., Saha, D., & Rabha, B. (2021). A Brief Review on Topical Gels as Drug Delivery System. Journal of Pharmaceutical Research International, 344–357. https://doi.org/10.9734/jpri/2021/v33i47a33020

[13]. European Pharmacopoeia (Ph. Eur.), 11th ed.; European Directorate for the Quality of Medicines and Health Care—EDQM: Strasbourg, France, 2022; Available online: https://www.edqm.eu/en/ (accessed on February 26, 2023).

[14]. Alvarez-Soria M.A., Herrero-Beaumont G, Moreno-Rubio J.et al.: " Long-term NSAID treatment directly deceases COX-2 and Mpges-1 production in the articular cartilage of patients with osteoatheritis,"ostroartherities and cartilage, 2008,16(12);1484-1493

[15]. Li.L,Rossoni G, Sparatore A, Lee L.C. Del Soldato P and MooreP.K. "Anti-inflammoraty and gastrointestinal effects of a novel diclofenac derivative, "Free Radial Bioalogy and Medicine, 2007,42(5);706-719.

[16]. Banker.G.S. and Rhodes. C.T., Moderen Pharmaceutics, 2nd Edn.,vol.40,MarcelDekker,inc,Madison avene .New York, 1990,303-307

[17]. S.Roychowdhury, D.H.Singh, R.Gupta, D.Manish, A Review on Pharmaceutical gel, Int. J. Pharma.Res. Bio. 2012, 1(5), pp21-36

[18]. K.Saroha, S.Singh, A.Aggarwal, S.Nanda, Transdermal Gels- An alternative vehicle for drug delivery, Int.J. Pharm. Chem. Biol. Sci. 2013, 3(3), pp495-503

[19]. Vijay Kumar Singh, Praveen Kumar Singh, Purnendu Kumar Sharma, Peeyush Kumar Srivastava, and AshutoshMishra.Formulation and evaluation of topical gel of Acelofenac containing piparine, Indo-American Journal of pharmaceutical research. 2013; 3(7): 5266–5280.

[20]. Florence AT, Attwood D. Physicochemical Principles of Pharmacy. Pharmaceutical Press, London, UK, 2011

[21]. Jain SK, Soni V. Bentley's Textbook of Pharmaceutics. Elsevier Health Sciences, India, 2012.

[22]. Florence AT, Attwood D. Physicochemical Principles of Pharmacy. Pharmaceutical Press, London, UK, 2011

[23]. Martinez MA, Gallardo J, Benavides MM, López-Duran JDG, Lara GV. Rheological behavior of gels and meloxicam release. Int J Pharm. 2007;333:17–23

[24]. Jain SK, Soni V. Bentley's Textbook of Pharmaceutics. Elsevier Health Sciences, India, 2012.

[25]. Uma devi, S., Ganesan, M. and Mohanta, G. P., Design and evaluation of tetracycline hydrochloride gels, Indian Drugs, 2002, 39(10), 552-554.