ISSN No:-2456-2165

Formulation And Evaluation of Salicylic Acid / Sodium Salicylate Topical Gels Using Peg Polymers

Terli Bhargavi Punyayathi
NRI College of pharmacy

Abstract:- Topical gels have advantages in the formulation to circumvent the first pass effect, to improve its bio availability, to reduce dosing frequency and dose related side effects. Sodium salicylate and salicylic acid are formulated as topical gels which is used as the keratolytic or anti-inflammatory agent. Topical gels of salicylic acid is a BCS class I drug were prepared by fusion method and characterized by testing for clarity, homogenesity, spreadibility, melting point, freezing point, surface pH, drug content uniformity and in-vitro drug dissolution studies. Nine formulations of salicylic acid and sodium salicylate topical gels are formulated at different ratios of polymers like poly ethylene glycols 400 and 4000 and evaluated.

Keywords:- *Salicylic Acid, Sodium Salicylate, Transdermal Gel, In-Vitro Drug Release Kinetic Studies, BCS Class I Drug.*

I. INTRODUCTION

Pharmaceutical semisolid preparations may be defined as topical products intended for application on the skin or accessible mucous membranes to provide localized and sometimes systematic effects at the site of application [1].

Semisolids constitute a significant proportion of pharmaceutical dosage forms; they serve as carriers for drugs that are topically delivered by way of the skin, cornea rectal tissue, nasal mucosa vagina, buccal tissue, urethral membrane and external ear lining [2]. A wide range of raw materials available for the preparation of semisolid forms. A part from the usual pharmaceutical ingredients such as preservatives, antioxidants and solubilizes, the basic constituents of a semisolid dosage form are unique to its compositions [3]. The choice of suitable raw materials for a formulations development is made on the basis of drug delivery requirements and the particular needs to impart sufficient emmoliency or other quasi-medicinal qualities in the formulations. Because of their peculiar theological behavior semisolids can adhere to the application surface for long periods before they washed off [4]. This property helps to prolong drug delivery at the application site. A semisolid dosage form is advantageous in terms of its easy application, rapid formulation, and ability to topically deliver a wide variety of drug molecules. Semisolid forms usually are intended for localized drug delivery [5]. In the past few years, however these forms also have been explored for a systemic delivery of various drugs [6].

Gels are defined as semi rigid system's in which the movement of depressing medium is restricted by an interacting three dimensional network of particular or solvated macromolecules of the dispersed phase [7].

The word "gel" is derived from gelation and both gel and "jelly" can be drawn back to the Latin gels for "frost" and gel are meaning "freeze" or "congeal". The USP defines gels (sometimes called jellies) as semisolid systems containing either suspensions made up of small inorganic molecules interpenetrated by a liquid [8]. Where the gel mass contains a network of small separate particles the gel is classified as a two phase system. In a two phase system, if the particle size of the dispersed phase is relatively large, the gel mass is sometimes called as a magma. In pharmaceutical applications water and hydro alcoholic solutions are most common. The formation of these inorganic gels is reversible [9].

There are several type's gels:-

Controlled release gels, organo gels, extended release gels, amphiphilic gels, hydrophilic gels, non-aqueous gels, bio adhesive gels, thermo sensitive sol-gel reversible hydrogels, complexation gels, hydrogels[10] .

A gel formulation includes a gelling agent carbomers, hydroxyl ethyl cellulose and hydroxy propyl cellulose are the most widely used and solubilizers. Depending on the excipients used a gel can be transparent (most common), translucent, or opaque [11].

Ideally, the gelling agent must be inert, safe and cannot react with other formulation constituents. The gelling agent should produce a sensible solid like nature at the time of storage which is easily broken exposed to hear force produced by squeezing the tube. It should have suitable anti-microbial agent. The topical gel must not be sticky. The ophthalmic gel must be sterile. The apparent viscosity or gel strength increases with an increases in the effective crosslink density of the gel. They exhibit the mechanical characteristics of the solid state. Each component in continuous throughout the system. There is high degree of attraction amongst the dispersed phase and water medium so the gels remain equally uniform upon standing and doesn't freely settle [12].

Non greasy application. Being easy to formulate with active ingredients. Adhering will to the application site. Being washable and non-toxic. Stability over time. Ability to target affected area for rapid treatment. Preventing unwanted side effects through bypassing the digestive system. Easy spreading. Skin retention. A cooling effect on the skin [13].

ISSN No:-2456-2165

Some drugs aren't absorbed easily through the skin. There's a possibility of an allergic reaction. The effect of gel's initiates slower (but lasts longer). Additives in the gel may irritate the skin. Application site must be monitored for reactions. Effectiveness may be impacted by temperature, humidity and other environmental factor's [14].

They are various methods include for the preparation of topical gels like fusion, cold and dispersion method [15].

II. MATERIALS AND METHODS

Materials used in these studies are salicylic acid and sodium salicylate are used as drugs for medicinal action. Poly ethylene glycols 400 and 4000 used as polymers.

Equipment's used for these studies are digital balance, electronic balance, colorimetry, magnetic stirrer and digital PH meter.

➢ *Preformulation studies:-*

Polyethylene glycol is a addition polymer of ethylene oxide and water. PEG grades 400 to 600 are liquids, grades 1000 and above are solids.

Liquid grades (PEG 200-600) occur as clear, colorless or slightly yellow colored, viscous liquids. They have a slight but characteristic odor and a bitter, slightly burning taste. PEG 600 can occur as a solid at ambient temperatures. Solid grades (PEG>1000) are white color and range in consistency from pastes to waxy flakes. They have a faint, sweet odor. Grades of PEG 6000 and above are available as free flowing milled powders [16].Aqueous solutions of higher-molecular weight grades may form gels. Liquid polyethylene are soluble in acetone, alcohols, benzene, glycerin and glycols[17].Solid polyethylene glycols are soluble in acetone, dichloromethane, ethanol (95%) and methanol; they are slightly soluble in aliphatic hydrocarbons and ether, but insoluble in fats, fixed oils and mineral oil [18].

III. ANALYTICAL METHODS

A number of methods are reported in the literature for the estimation of salicylic acid. Colorimetric method was used for the estimation of salicylic acid at 540 nm in water.

➢ *Standard solutions:-*

100 mg of salicylic acid was dissolved in q.s water in a 100 ml volumetric flask (A), and the solution was made up to the mark with water. The concentration of the stock solution is 1 mg per ml of solution or 1000 µg per ml solution.

➢ *Procedure:-*

The prepared stock solution suitably diluted with water to obtain a series of standard solutions containing 50, 100, 150, 200 and 250 µg of salicylic acid per ml. The absorbance of the solutions was measured at 540 nm using ELICO colorimeter. Water was used as a blank.

➢ *Preparation method*

In these studies gel was prepared by fusion method. Weigh required amount of PEG 400 in the clean 00dry beaker to that add required amount of PEG 4000 and dissolve it by heating until clear solution occurs. Then to that add 1g of salicylic acid with continuous stirring and allow it to cool.

IV. RESULTS

Table-1:-**Different formulation's of gel's**: - The formulation for the salicylic acid gels are shown

S no.	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1.	Salicylic acid (g)	1	1	1	1	1	1	-	-	-
2.	Sodium salicylate (5g/10ml H2O)	-	-	-	-	-	-	2ml	2ml	2ml
3.	PEG 400 (g)	2	3	4	5	7	8	2	4	7
4.	PEG 4000 (g)	7	6	5	4	2	1	7	5	2

➢ *Calibration curve of salicylic acid by colorimeter:-*

The absorbance of the various concentrations of salicylic acid solutions are given in the table. The absorbance were plotted against the concentrations of the salicylic acid. This calibration curve was used to determine the amount of salicylic acid in unknown solutions. This was shown in table-2

Table-2 Absorbance of Standard Salicyclic Acid Solutions

S NO	Concentration µg/ml	Absorbance at 540 mm			Average
		Trail 1	Trail 2	Trail 3	
1	50	0.15	0.14	0.15	0.15
2	100	0.32	0.33	0.31	0.32
3	150	0.44	0.44	0.42	0.44
4	200	0.62	0.63	0.62	0.62
5	250	0.84	0.83	0.84	0.84

ISSN No:-2456-2165

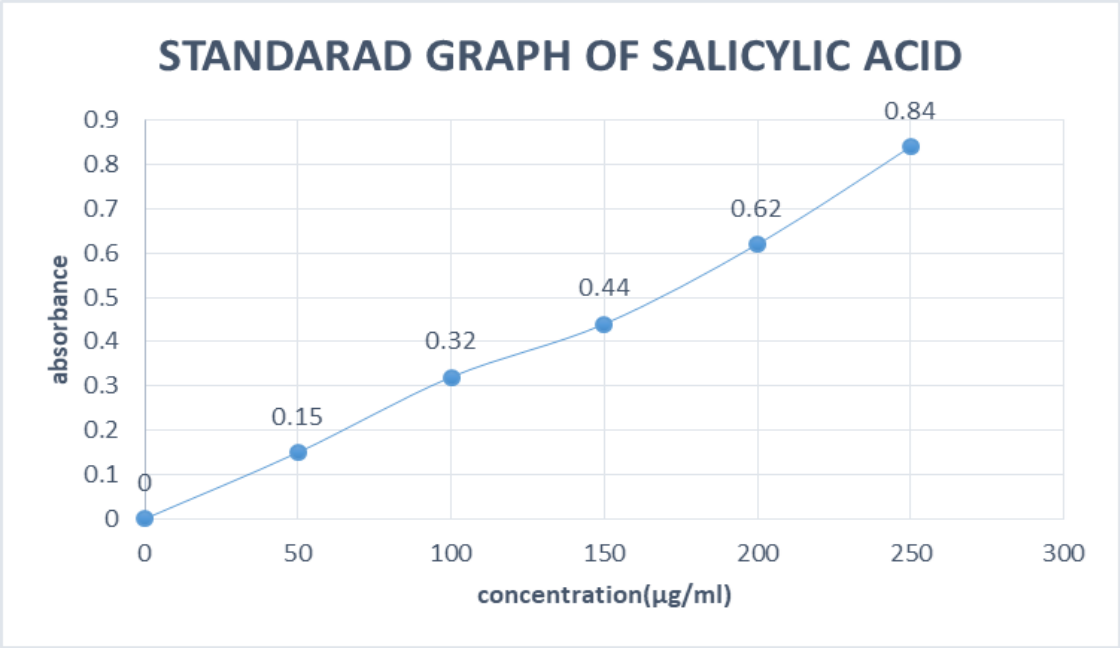

Fig 1 Standarad Graph of Salicylic Acid

From the graph we determine that, y=-0.0038x-0.0143 and its R^2 is 0.993.

The drug release profile and their evaluation parameters of all formulations of salicylic acid and sodium salicylate topical gels are shown in the table 3 &4.

Table 3 Drug release profile of all formulations of salicylic acid and sodium salicylate topical gels

S NO	Time minutes	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	15	15.10%	17.97%	19.47%	21.42%	14.80%	18.21%	14.73%	31.24%	30.48%
2	30	31%	34.64%	40.25%	42.37%	43.61%	43.54%	35.88%	56.24%	54.60%
3	45	44.56%	50.43%	55.84%	58.09%	62.54%	63.99%	51.27%	65.27%	69.49%
4	60	54.64%	63.59%	66.66%	69.51%	74.07%	78.65%	62.17%	75.69%	79.38%
5	75	65.5%	73.68%	77.73%	77.13%	79.01	86.21%	68.58%	79.16%	80.13%
6	90	70.54%	78.94%	75.76%	79.52%	81.48%	89.77%	71.78%	83.33%	84.39%
7	105	74.8%	82.45%	79.65%	84.28%	84.35%	92.88%	73.06%	83.33%	87.22%
8	120	79.25%	87.48%	79.65%	84.28%	86.41%	95.10%	73.06%	84.02%	88.34%

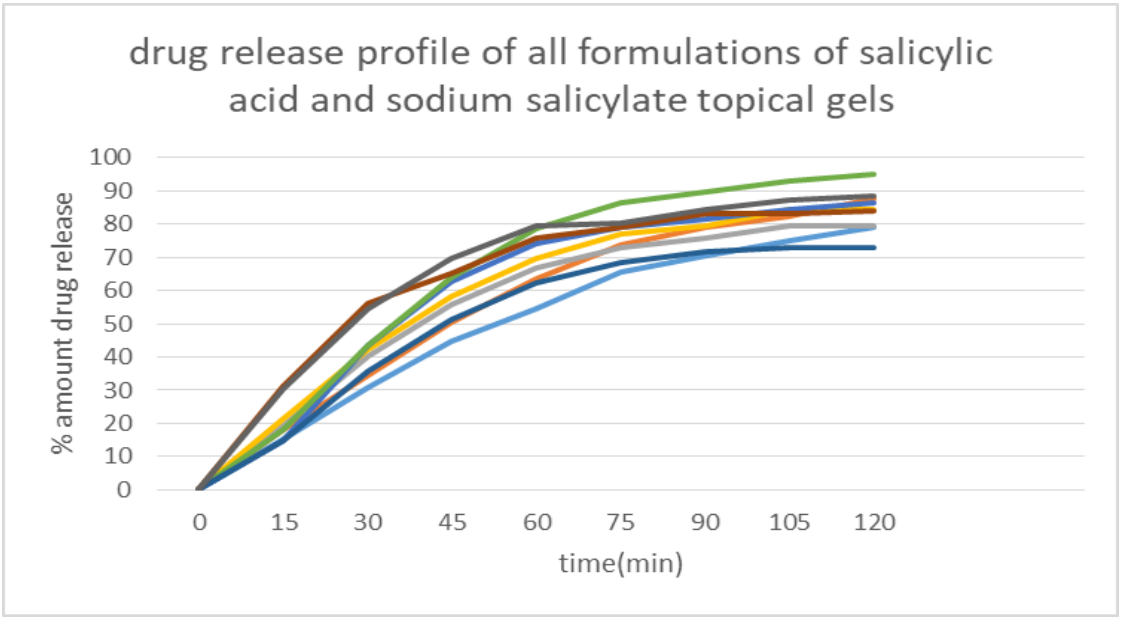

Fig 2: Evaluation parameters of all the formulation topical gels of salicylic acid and sodium salicylate

ISSN No:-2456-2165

Table 4 Evaluation parameters of all the formulation topical gels of salicylic acid and sodium salicylate

Parameters	F1	F2	F3	F4	F5	F6	F7	F8	F9
Assay(mg)	113.15	100	101.30	92.10	106.57	98.68	68.42	63.15	61.84
Rate constant(k_1/min)	0.0133	0.0177	0.0142	0.0165	0.01773	0.0264	0.01197	0.015	0.0177
Half life(t1/2)(min)	51.91	48.80	42	39.15	39.08	26.25	57.86	44.25	39.07
T_{90}(min)	172.30	130.11	162.18	139.57	129.89	87.23	192.39	147.06	129.89
Spreadability($cm^{\wedge 2}$)	2.6	2.85	3.1	3.6	-	-	3.25	4.35	
Ph	1.80	1.91	1077	1.77	1.78	2.27	1.78	1.92	1.79
Melting point(^{0}C)	44	39	37	37	32	29	37	32	28
Freezing point(0C)	38	36	34	33	25	23	32	28	20

V. DISCUSSION

1. The chemical reactivity of polyethylene glycols is mainly with the two terminal hydroxyl groups, which can be either esterified or etherified. All grades of PEG's undergoes auto oxidation in the presence of peroxide impurities.
2. Liquid and solid PEG's may be incompatible with some coloring agents. PEG's reduces the antibacterial activity of antibiotics such as penicillin, bacitracin [19].
3. The preservative efficacy of the parabens may also impaired by binding with PEG's. It shows incompatibility it causes discoloration of the sulfonamides and dithranol; sorbitol may be precipitated.
4. Plastics such as polyethylene, phenol formaldehyde, and poly vinyl chloride and cellulose-ester membranes (in filters) may be dissolved or softened by polyethylene glycols. Migration of PEG's can occur from tablet coatings, and leads to interaction with core components [20].
5. From the table F4 is the best formulation.
6. Comparatively according to drug release studies of formulation F5, F6 and F9 are faster than F4 formulation gel but they are unstable at room temperature due to its lower melting point.
7. Even F5, F6 and F9 a formulation's drug release faster than the F4 formulation, but F4 is the best formulation because F5, F6 and F9 have the lowest melting point due to highest ratio of PEG 400 and these formulation's get liquefied before reaching to the body temperature. Hence F4 is correct formulation in its melting point range and better spreadibility.
8. After these three formulations the drug release fastest for F4 so from this best formulation is F4.
9. During the spreadability test the formulation F5, F6, and F9 are unpredictable due separation of oily substance from the gel.
10. Since they are unstable when compared to other formulations at room temperature.

VI. CONCLUSION

At present research is concerned with formulation and evaluation of transdermal gels of salicylic acid. Nine different formulations were developed with varying Concentrations of polymers like PEG 400 and PEG 4000. The gels were formulated and evaluated for best formulation.

All together the nine formulations were made. In that formulations, F4 was found to be best one in terms of vitro drug release. F4 gel contained PEG 400 at a concentration of 50% and PEG 4000 concentration of 40%. Hence a gel of F4 was formulated which is better than the other eight formulations.

REFERENCES

[1]. Niyaz Basha B, Kalyani Prakasam, Divakar Goli, Formulation and Evaluation of Gel containing Fluconazole anti fungal agent. October 2011; Research gate.
[2]. Mazher Ahmed Md, Review article on topical gel formulation; Journal of Pharmaceutical Quality Assurance.
[3]. Patil PB, Datir SK, Saudagar RB, A review on Topical Gel's as drug delivery and therapeutics. Volume -9 no 3-5, 2019 volume.
[4]. Loveleen Preet Kaur, Rajeev Garg, Gupta GD, Topical gel's review. Volume 3, issue-1, 2022, Research Journal of Pharmacy and Technology.
[5]. Bhushan Rajendra Patil, Anup Mukund Akarte, Pankaj Motilal Chowdari, Kalpesh Shamkanth Wagh ,Prakash Hiraman Patil, Development and characteristics of topical gel containing Nimesulide. GSC Biological and Pharmaceutical Sciences; 2021.
[6]. Vijay Singh, Praveen Kumar Singh, Peeyush Kumar Srivastava, Purnendu Kumar Sharma, Formulation and Evaluation of topical gel of Aceclofenac containing Piparine. Research Gate; July 2013.
[7]. Jani Rupal, Jani Kaushal, Chitral Mallikarjuna Setty, Dipti Patel, Preparation and Evaluation of topical gel of Valdecoxib. January 2010; International Journal of Pharmaceutical Sciences and Drug Research.
[8]. Nikunjana Patel A, Natvar Patel J, Rakesh Patel P, Formulation and Evaluation of Curcumin Gel for Topical Application. volume 14, 2009, Issue 1, Pharmaceutical Developememt and Technology.
[9]. Mei Chen X, Kemeth Alexander S, Grabriella Bakis, Formulation and Evaluation of anti-bacterial creams and gels containing metal ions for Topical applications. Volume 2016 Article ID 5754349; Journal of Pharmaceutics.
[10]. Rajashekaran Aiyalu, Arulkumaran Govindarajan, Arivukkarasu Ramaswamy; Formulation and Evaluation of Topical Herbal Gel for the Treatment of Arthritis in Animal Model. Volume 52; July-September 2016; Brazilian Journal of Pharmaceutical Sciences.

[11]. Akhilesh Chandra, Geetha Aggarwal, Satish Machanda, Akhay Narula; Volume7, issue 5, 2019; Pharmaceutical Nanotechnology, Development of Topical Gel's of Methotrexate incorporated ethosomes and Salicylic acid for the Treatment of Psoriasis.
[12]. Poonam Madhukar Kasar, Kalyanisudar Rao Kale, Dipti Ganesh Phadtare; Volume 10, Issue 4 (july-august) 2018; International Journal of Current Pharmaceutical Research.
[13]. Upendra Nagaieh, Promila Sharan, Rajeev Kumar, Spriya Sharan, Neha Gulati, Amit Chaudhary; Development and Characterization of anti-aging Topical Gel; Journal of Advanced Pharmacy Education and Research.
[14]. Bhalke A, Kirloskar GV, Bhutada RR, Jagtap NK, Giri MA, 2019; Design, Development and Evaluation of Topical Anti Inflammatory Herbal Gel. International Journal of Pharmaceutical Sciences and Research.
[15]. Vishwanath Abasaheb Bose, Avinash Balasaheb Gangude, Anil Bhavrao Deore, 2019; Formulation and Evaluation of ant-bacterial topical gel of Doxycycline Hyclate, Neem oil and tea tree oil.
[16]. Pradal J, Vallet CM, Frappin G, Bariguian F, Lombardi MS; 2018; Importance of the Formulation in the Skin Delivery of Topical Diclofenac. Dovepress. Open Access to Scientific and Medical Research.
[17]. Arjun Gaire, Sangit Maharajan, Sumitra Shrestha, Naresh Thapa, Dr. Jeevan Raj Shrestha; 2021; Formulation and Evaluation of Fluconazole Gel for the Topical Drug Delivery System; American Academic Scientific Research Journal of Engneering, Technology and Science.
[18]. Indian Pharmacoepia Edition 2010
[19]. Maru SM, Manvi FV, 2005; Formulation and Evaluation of Temoxicam Gel's for Topical use. The East and Central African Journal of Pharmaceutical Sciences.
[20]. Hiren Patel, Mital Panchal S, Suresh Shah, Dr. Vadalia KR, 2012; Volume 1; Formulation and Evaluation of Transdermal Gel of Sildenafil Citrate. International Journal of Pharmaceutical Research and Allied Sciences.
[21]. Sravani Kota, Mohammed Asadullah Jahangir, Mazher Ahmed MD, Imarn Kazmi, Durga Bhavani P, Development and Evaluation of Ofloxacin Topical Gel. Scholar's Research Library.