Panacea Journal of Pharmacy and Pharmaceutical Sciences 2018:7(1);719-728

International Journal

Panacea Journal of Pharmacy and Pharmaceutical Sciences
ISSN: 2349 7025

PJPPS
Panacea Research Library
http://internationaljournal.org.in/journal/index.php/pjpps

Research Article **Volume 7 Issue 1**

FORMULATION AND EVALUATION OF MEFENAMIC ACID GEL FOR TOPICAL DELIVERY

Nehal Sandanshi, Devashish Rathore*, Rashmi Dahima
School of Pharmacy, Devi Ahilya Vishwavidyalaya, Taksashila Campus, Khandwa Road, Indore-452001, M.P., India

Article history:

Received:
6th April 2018
Received in revised form:
20th April 2018
Accepted:
24th April 2018
Available online:
25th April 2018

Corresponding author:
Devashish Rathore

Email address:
devashish28@yahoo.com

***Present address*:**
School of Pharmacy, Devi Ahilya Vishwavidyalaya, Indore, India

These author(s) have no conflict of interest to declare.

Abstract:

Objective: Mefenamic acid is an anthranilic acid derivative and is used to treat pain, including menstrual pain. Wide choice of vehicles ranging from solids to semisolids form has been used for skin care and topical treatment of dermatological disease. The objective of the study was to prepare gel of Mefenamic acid, a NSAID, using Carbopol 940, Carbopol 934, mixture of Carbopol 934 and 940 and Carboxymethylcellulose (CMC) as a gelling agent.

Methodology: Gel formulations were prepared and characterized for appearance, pH determination, spreadability, homogeneity and grittiness, extrudability, drug content and release.

Results: The drug content was found to be 90.68%, 92.31% and 91.54% for Carbopol 940, Carbopol 934 and mixture of Carbopol 940 & 934 respectively. The sustained releases from all the prepared gel formulation were observed. The cumulative percent releases at 120 minutes were found to be 96.03%, 82.99% and 92.43% for Carbopol 940, Carbopol 934 and mixture of Carbopol 940 and 934 respectively.

Conclusion: The oral use of Mefenamic acid is not much recommended as it has many side effects. Commercially Mefenamic acid topical gel preparation are not available in the market, thus this formulation is made for better patient compliance and to reduce the dose of drug and to avoid the side effects like liver damage and kidney damage.

Keywords: Gel, Mefenamic acid, Carbopol 940, Carbopol 934, Topical drug delivery

Introduction

Several analgesic preparations are available in the market as different topical preparations. Mefenamic acid, an effective NSAID has always been used as an anti-inflammatory and analgesic agent. Conventionally it is available in the form of tablets and suspensions. Most of the topical preparations are used for the localized effects at the site of their application by virtue of drug penetration into the underlying layers of skin or mucous membranes [1]. Skin is one of the most accessible organ of human body for topical administration and main route of topical drug delivery system [2].

Among the topical formulations a wide choice for the treatment from solid dosage to semisolid doses forms and to liquid dosage formulation the transparent gels have widely accepted in both cosmetics and pharmaceuticals. There are various medicated products that are applied to the skin. Such products are referred as topical or dermatological products [3].

Number of medicated products is applied to the skin or mucous membrane that either enhances or restores a fundamental function of a skin or pharmacologically alters an action in the underlined tissues. Such products are referred as topical or dermatological products [2, 4]. Hydroxypropyl methylcellulose (HPMC), Carbopol 940, Carbapol 934, Carboxymethyl cellulose (CMC), Sodium alginate has been used as hydrophilic polymers topically in gel drug delivery system. A series of grades based on molecular fractions of these polymers are used at a concentration between 1 to 5% in topical gel formulation. The application of medicinal substance to the skin is a concept doubtless as humanity [5-6].

Mefenamic acid is an anthranilic acid derivative. Mefenamic acid is a non steroidal anti-inflammatory drug which is poorly water soluble. It is slightly soluble in methanol and ethanol. It is used to treat pain, including menstrual pain. Mefenamic acid decreases inflammation (swelling) and uterine contractions by a still-unknown mechanism. However it is thought to be related to the inhibition of prostaglandin synthesis.

At the present time, it is used only in the form of oral preparations or suppositories exhibiting excellent anti-inflammatory and analgesic effects when so administered. However, side effects such as stomach and intestine problems, liver problems and kidney problems may occur, especially upon oral administration. Therefore, anti-

inflammatory and analgesic preparations which are absorbed cutaneous without showing such side effects are desired.

Gels are defined as "semisolid system in which a liquid phase is constrained within a polymeric matrix in which a high degree of physical and chemical cross-linking introduced" [7].

Material and Method

Materials

All chemicals used were of analytical grade. Mefenamic acid (Aristo Pharmaceutical Ltd, Mandideep), Carbopol 940 (SD Fine Chem. Ltd. Mumbai), Carbopol 934 (LOBA Chemie Pvt. Ltd.), Ethanol (Merck) and Triethanolamine (Merck) were used for this work.

Preparation of Standard graph of drug

Ten mg of mefenamic acid was accurately weighed, some amount of methanol was added to dissolve the drug and then volume was made up to 10 ml by phosphate buffer of pH 7.4. From this stock solution, 1 ml was withdrawn and transferred into 10 ml volumetric flask. Volume was made with buffer in order to get standard stock solution containing 100 µg/ml. Form this standard stock solution, a series of dilution (5, 10, 15, 20, 25 µg/ml) were prepared. The absorbance of these solutions was measured spectrophotometrically against blank of phosphate buffer of pH 7.4 at 285 nm for mefenamic acid (Figure1).

Preparation of mefenamic acid gel

Mefenamic acid (50 mg) was dissolved in 95% ethanol (10mL) while stirring. On the other hand, carboxyvinyl polymer like carbopol 940 (F1), carbopol 934 (F2), mixture of carbopol 940 & 934 (F3) were mixed with distilled water (2g) uniformly under stirring. Then Triethanolamine (1 mL) was added to the mixture with continuous stirring. To this gel base, the previously prepared alcoholic solution of mefenamic acid was added and the whole was adjusted to 5g by further adding purified water. After stirring well, a gel preparation having a pH of 6.5 was obtained. The different batches prepared are shown in table 1.

Table 1. Composition of gel preparation

Ingredients	F1	F2	F3	F4
Mefenamic acid (mg)	50	50	50	50
Carbopol 940 (mg)	50	-	25	-
Carbopol 934 (mg)	-	50	25	-
Carboxymethyl cellulose (mg)	-	-	-	50
Triethanolamine (mL)	1	1	1	1
Ethanol (mL)	10	10	10	10
Water (mL)	q.s.	q.s.	q.s.	q.s.

Evaluation of mefenamic acid gel [8-9]

Physical evaluation

All the formulations were evaluated for colour, occulsiveness, washability, phase separation and odour. (Table 2)

Determination of pH

The pHs of the formulated gels were determined using digital pH meter. The electrode was immersed in the gel and readings were recorded from pH meter. (Table 3)

Spreadability

A sample of 0.1 g of each formula was pressed between two slides (divided into squares of 5 mm sides) and left for about 5 minutes where no more spreading was expected. Diameters of spreaded circles were measured in cm and were taken as comparative values for spreadability. The results obtained are average of three determinations. (Table 4)

Homogeneity and grittiness

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates. Also, the homogeneity can be detected when a small quantity of the gel is

rubbed on the skin of the back of the hand. The grittiness of prepared gel is also observed in the same manner. (Table 5)

Extrudability study

The extrudability of gel formulations were determined by filling gel in the collapsible tubes. The extrudability was determined in terms of weight in grams required to extrude a 0.5 cm ribbon of gel. (Table 6)

Drug content

A specific quantity (100 mg) of developed gel was taken and dissolved in 100 ml of phosphate buffer of pH 7.4. The volumetric flask containing gel solution was shaken for 2 hr on mechanical shaker in order to get complete solubility of drug. This solution was filtered and estimated spectrophotometrically at 285 nm using phosphate buffer (pH 7.4) as blank. (Table 7)
Drug content was calculated by the following formula:
Drug content= (Absorbance x Dilution factor) / (Slope x 1000)

In vitro release studies

The *in vitro* drug release studies were carried out using an egg membrane. The formulation was applied on membrane which was placed in the test tube and it was tied with the help of thread on the burette stand. Phosphate buffer pH 7.4 was used as a dissolution media. The temperature of the beaker containing phosphate buffer was maintained at 37 °C. This whole assembly was kept on a magnetic stirrer and the solution was stirred continuously using a magnetic bead. Sample (10 ml) was withdrawn at suitable time intervals and replaced with equal amounts of fresh dissolution media. Samples were analyzed spectrophotometrically at 285 nm and the cumulative % drug release was calculated. (Table 8)

Result and Discussion

The formulation of mefenamic acid gel by CMC (F4) as polymer was not prepared, as alcohol has less potency in Water. All developed gel showed occulsiveness. No odour and phase separation were observed. All preparations were found to be washable. The

pH values of all developed gels were obtained in between 6.0-6.7. All developed gel showed good homogeneity with absence of lumps and no grittiness. The preparations are considered to be good if it takes minimum time to spread on the surface. The values of spreadability indicate that the gel is easily spreadable by small amount of shear. Extrusion of gel from the tube is important during application and for the patient compliance. The values of extrudability of different formulations were found good. Drug content uniformity of all formulations was observed in the ranges from 90-92%. The drug content was found to be 90.68%, 92.31% and 91.54% for Carbopol 940, Carbopol 934 and mixture of Carbopol 940 & 934 respectively. In vitro release of formulation showed that the release was comparable to each other. The sustained releases from all the prepared gel formulation were observed. The cumulative percent releases at 120 minutes were found to be 96.03%, 82.99% and 92.43% for Carbopol 940, Carbopol 934 and mixture of Carbopol 940 & 934 respectively (Figure 2).

Table 2. Physical evaluation of formulations

S. No.	Formulation Code	Colour	Occulsiveness	Washability	Phase separation	Odour
1	F1	White	Yes	Washable	No	No
2	F2	White	Yes	Washable	No	No
3	F3	White	Yes	Washable	No	No

Table 3. pH of various formulations

S. No.	Formulation code	pH
1	F1	6.4
2	F2	6.1
3	F3	6.3

Table 4. Spreadability of various formulations

S. No.	Formulation Code	Diameter (cm)
1	F1	4.2
2	F2	4.1
3	F3	4.3

Table 5. Homogenity and grittiness of various formulations

S. No.	Formulation Code	Homogenity	Grittiness
1	F1	Yes	No
2	F2	Yes	No
3	F3	Yes	No

Table 6. Extrudability of various formulations (-not good, +good)

S. No.	Formulation Code	Extrudability
1	F1	+
2	F2	+
3	F3	+

Table 7. Drug content of various formulations

S. No.	Formulation Code	Drug content (%)
1	F1	90.68
2	F2	92.31
3	F3	91.54

Table 8. *In vitro* drug release of various formulations

Time (min)	F1	F2	F3
0	0	0	0
10	21.67±3.2	15.33±4.66	18.07±6.83
20	34.92±2.88	25.81±4.19	29.39±1.22
30	51.23±7.55	37.37±6.68	42.77±6.11
60	68.55±4.24	49.22±3.32	57.14±4.44
90	82.75±1.70	63.10±5.75	73.09±1.20
120	96.03±1.45	82.99±1.89	92.43±0.49
180	-	93.62±2.29	-

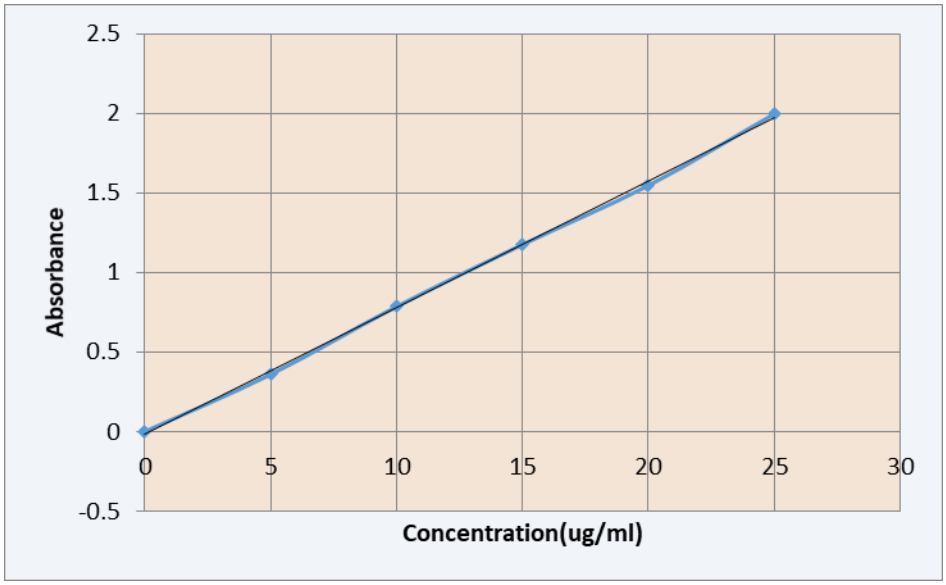

Figure 1. Standard graph of drug

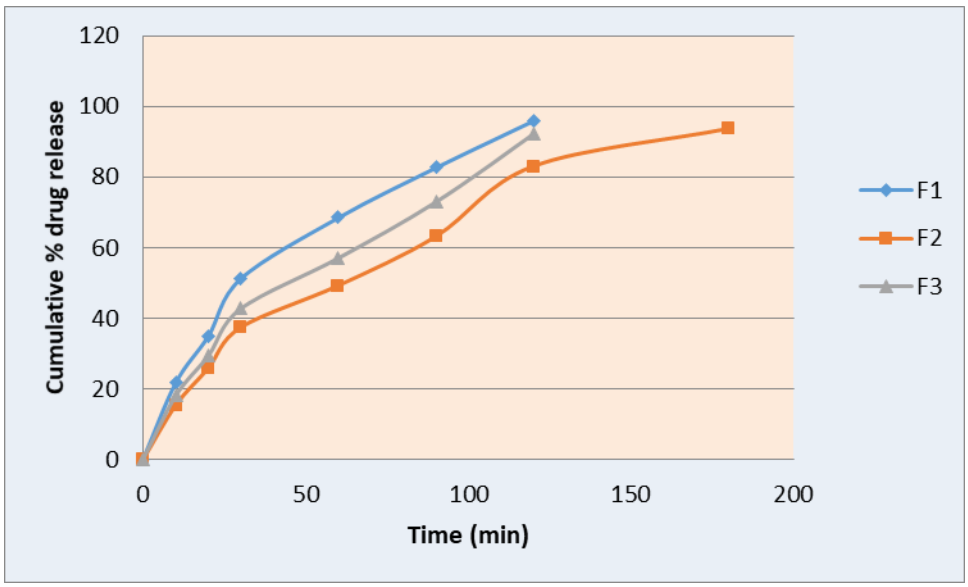

Figure 2. *In vitro* cumulative % drug release of formulation F1-F3

Conclusion

Mefenamic acid is an anthranilic acid derivative and an attempt to develop the formulation of gel was successfully done. The prepared formulation shown excellent drug release behavior up to 180 minutes. In coming years, topical drug delivery will be extensively used to impart better patient compliance.

References

1. Lionberger, D.R., Brennan, M.J. (2010) Topical nonsteroidal anti-inflammatory drugs for the treatment of pain due to soft tissue injury: diclofenac epolamine topical patch. Journal of Pain Research, 3, 223– 233.
2. Provost C. (1986) Transparent oil-water gels: A review. International Journal of Cosmetic Science, 8(7), 233-247.
3. Jain N.K., Misra, A.N., Controlled and Novel Drug Delivery (2005) CBS Publishers and Distributors, New Delhi.
4. M.S. Rashmi (2008) Topical gel: A review, Pharmaceutical Review, 6(3), 244-249.
5. Shivhare U.D., Jain K.B., Mathur V.B., Bhusari K.P., Roy A.A. (2009) Formulation development and evaluation of diclofenac sodium gel using water soluble polyacrylamide polymer. Digest J Nanomet and Biostruct. 4(2), 285-290.
6. Golinkin H.S. (1979) Process for fracturing well formulation using aqueous gels, US patent 4137182.
7. Bharadwaj, S., Gupta, G.D., Sharma V.K. (2012) Topical gel a noval approach for drug delivery, J of Chem, Biol and Phys sci, 2(2), 856-867.
8. Chauhan, T., Parashar, B., Arora S. (2013) Design and Evaluation of Diclofenac Sodium Gel. Int J of Pharm Sci, 2(1), 72-81.
9. Oswal, T., Naik, S. (2014) Formulation and evaluation of mefenamic acid emulgel. Int J of Pharm Res and Dev, 5 (12), 91-100
10. Skin anatomy and physiology. http://www.essentialdayspa.com/epidermis-c17.httm (Online).
11. Noreen H. (2005) Anatomy and physiology of the skin. Dermatol Nurs, 17(1), 62.
12. Stanely S. (2004) Transdermal drug delivery. Mol Interv ,4(6),308-12.
13. Girish C. (2006) Transdermal drug delivery systems. A review (Online).
14. Ansel, H.C., Allen Jr, L.V., Popovich, N.G., (1999) Pharmaceutical Dosage Forms and Drug Delivery Systems, 7th ed. Lippincott Williams and Wilkins, New York.
15. Baksh, A., Shaikh, A., Bhargava, T., Singh, S. (2012) Formulation and in-vitro evaluation of NSAID's gel. Int J of Current Pharm Res, 4(3), 56-58
16. Basha, B.N., Prakasam, K., Goli, D., (2011) Formulation and evaluation of gel containing fluconazole antifungal agent. Int J of Drug Dev and Res, 3(4), 109-128.

17. Parashar, B., Kabra, A., Chandel A., (2013). Formulation and Evaluation of Gel Containing Miconazole Nitrate an Antifungal Agent. Int J of Pharma Res & Rev, 2(6), 18-28.
18. Baviskar, D., Kumar, Y., Biranwar, A., Bare, K., Parik, VB., Sapate, M., Jain, DK. (2013) *In Vitro* and *In Vivo* Evaluation of Diclofenac Sodium Gel Prepared with Cellulose Ether and Carbopol 934P. Tropical J of Pharm Res, 12 (4), 489-494.
19. Indian Pharmacopoeia. Ministry of Health and Family Welfare, New Delhi, India. 2007, 1: 148, 289, 1020.
20. Khullar, R., Kumar, D., Seth, N., Saini, S. (2012) Formulation and evaluation of mefenamic acid emulgel for topical delivery. Saudi Pharm J., 20, 63-67.
21. Robinson, J.R., Lee, H.L. Vincent, Controlled Drug Delivery, Marcel Dekker, Inc., Madison Avenue, New York, 2(29), 524-526.

How to cite this article:
Nehal Sandanshi, Devashish Rathore, Rashmi Dahima. Formulation and evaluation of mefenamic acid gel for topical delivery; *Journal of Pharmacy and Pharmaceutical Sciences 2018:7(1);719-728.*