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RESEARCH PAPER

PREPARATION & CHARACTERIZATION OF TOPICAL GEL CONTAINING SANDALWOOD OIL OF NAPROXEN FOR THE TREATMENT OF RHEUMATOID ARTHRITIS

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Abstract

Naproxen is a propionic acid derivative of group NSAIDs i.e. non-steroidal anti-inflammatory drug used in various inflammatory conditions. The present research study is based on development of a topical gel formulation of naproxen containing sandalwood oil. The oral administration of naproxen comes with potential gastrointestinal disorders which can be avoided by delivering the drug to the inflammation site at a sustained, concentrated level over an extended period of time. Sandalwood oil, ethanol and carbopol 940 were used in different ratios for preparation of topical gel formulations. Sandalwood oil is used to reduce inflammation and gives soothing and cooling effect. There were six different formulations prepared and characterized in terms of grittiness, pH, drug content, homogeneity and viscosity. The physical compatability was confirmed by drug-excipients compatibility test. Keshary Chien K-C type of diffusion cell was used for the in-vitro drug diffusion studies by using a cellophane membrane. The cumulative present drug release was found to be 99.33% in 3 hours from F3. The overall study suggests that formulae F3 can be used in Naproxen gel preparation using sandalwood oil, which can be an effective drug delivery system in the treatment of rheumatoid arthritis since it relives the side effects of naproxen.

Keywords

Topical Gel, NSAIDs, Naproxen, Sandalwood oil

INTRODUCTION

Gel is defined as a semisolid system consisting of dispersion made up of either small inorganic particle or large organic molecule enclosing and interpenetrated by liquid. The inorganic particles form a three-dimensional "house of cards" structure. Gels consist of two-phase system in which inorganic particles are not dissolved but merely dispersed throughout the continuous phase and large organic particles are dissolved in the continuous phase, randomly coiled in the flexible chains." (Abrar *et al.*, 2012, Chandel A et al., 2013)

Inflammation is the human body's instantaneous reaction to loss to its cells and tissues by pathogens and other stimuli like chemicals or physical damage. It is the first response to immune system for infection or irritation. Inflammation can be illustrated by redness, heat, swelling, pain and loss of function of organ. These are termed as rubor, calor, tumor and dolor.

Naproxen is a propionic acid derivative related to the aryl acetic acid group of non-steroidal anti inflammatory drugs. It is White to creamy white, crystalline solid powder. Its half life is 12–24 hours. It comes under the Cyclooxygenase Inhibitors and Gout Suppressants category. Its marketed preparations available are aleve, anaprox, antalgin, apranax, Naproxen is a member of the aryl acetic acid group of non-steroidal anti-inflammatory drugs (NSAIDs). (Tambade et.al 2014) Naproxen has analgesic and antipyretic properties. The mechanism of action of naproxen, like that of other NSAIDs, is believed to be associated with the inhibition of cyclooxygenase activity. In this study, Naproxen topical gels were formulated using polymer carbopol940 and were evaluated with different studies. (Florey Klaus 1992)

MATERIALS AND METHODS

Preparation of Gel:

Naproxen drug (2%) dispersed in propylene glycol then carbopol P940 were finely dispersed in propylene glycol drug solution and water and stirred continuously at 300 rpm for 3 hrs. Then, lastly added sandalwood oil drop wise and mixed for 1 hour. The formulations of different gel preparation are listed in table 1.

Table no. 1 Ingredient Table

S. No.	Ingredients	Formulations (Quantity %)					
		F1	F2	F3	F4	F5	F6
1	Naproxen	200 mg (2%)	200 mg (2%)	200 mg (2%)	200 mg (2%)	200 mg (2%)	200 mg (2%)
2	Carbopol P 940	50 mg (0.50%)	75 mg (0.75%)	100 mg (1%)	125mg (1.25%)	150mg (1.50%)	175mg (1.75%)
3	Sandalwood oil	0.2 ml	0.4 ml	0.6 ml	0.8 ml	0.10ml	0.12 ml
4	Ethyl alcohol	6.0ml	6.0ml	6.0ml	6.0ml	6.0ml	6.0ml
5	Water	qs	qs	qs	qs	qs	Qs

Drug Diffusion Studies:

The drug diffusion studies of prepared gel were carried out in Keshary Chien diffusion cell using semipermeable membrane, attached to the diffusion cell such that the cell's drug releasing surface towards the receptor compartment which was filled with phosphate buffer solution of pH 6.8 at 37°C±2°C. The solution was continuously stirred. The sampling was done in 15 minutes of time interval i.e. 5 ml of the aliquots were withdrawn and the same volume was replaced with phosphate buffer of pH 6.8. The samples were analyzed for drug content using UV spectrophotometer at 317nm. The observations are shown in table No.2& there corresponding graph are shown in figure No1 & 2.

Table no. 2 % CDR formulation of F1, F2, F3, F4, F5& F6

S. No.	Time (min)	Formulation					
		F1	F2	F3	F4	F5	F6
1	0	0.0±0.00	0.0±0.00	0.0±0.00	0.0±0.00	0.0±0.00	0.0±0.00
2	15	11.55±0.15	9.03±0.36	12.05±0.17	11.54±0.14	12.75±0.26	12.68±0.18
3	30	16.75±0.17	14.25±0.24	27.80 ±0.3	17.75±0.19	24.57±0.25	21.86±o.39
4	45	23.92±0.28	22.05±0.42	31.33±0.24	21.32±0.28	34.43±0.40	29.39±0.29
5	60	30.22±0.25	21.33±0.40	37.41±0.40	28.99±0.22	38.57±0.40	36.57±0.44
6	75	41.61±0.36	32.40±0.15	45.71±0.23	35.98±0.39	46.93±0.15	41.19±0.25
7	90	50.63±0.30	46.48±0.45	51.23±0.12	43.03±0.37	55.73±0.47	59.73±0.18
8	105	62.73±0.24	52.33±0.43	66.03±0.37	51.19±0.28	69.24±0.45	63.23±0.31
9	120	71.40±0.38	61.17±0.20	75.36±0.35	59.43±0.33	74.82±0.20	74.82±0.34
10	135	84.62±0.41	77.82±0.35	87.33±0.56	66.39±0.42	79.39±0.35	81.22±0.56
11	150	82.33±0.45	72.45±0.51	91.66±0.40	73.45±0.47	86.95±0.50	86.95±0.49
12	165	90.11±0.40	82.29±0.30	93.62±0.63	83.04±0.39	91.51±0.30	90.45±0.62
13	180	91.51±0.75	86.92±0.87	99.27±0.45	90.33±0.67	95.06±0.88	96.17±0.49

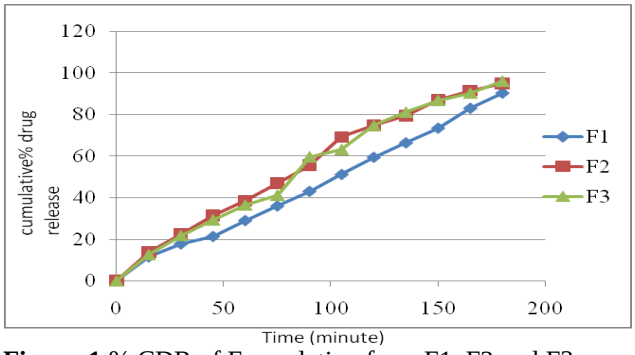

Fig no. 1 % CDR of Formulation from F1, F2 and F3

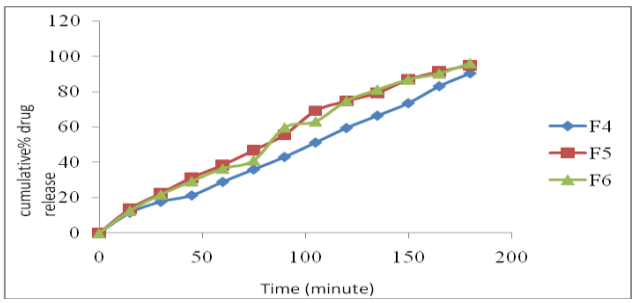

Fig. no. 2 % CDR of Formulation from F4, F5 and F6

EVALUATION OF GEL

1. Determination of Homogeneity

After the gels have been set in the container, all developed gels were tested for homogeneity by visual inspection. They were tested for their appearance and presence of any aggregates.

Table no. 3

Formulation	Homogeneity
F1	+++
F2	+++
F3	+++
F4	+++
F5	+++
F6	+++

The + sign indicated the confirmation of good homogeneity that is free from any lumps and also have good elegance effect.

2. Grittiness

All the formulations were evaluated microscopically for the presence of any appreciable particulate matter which was seen under light microscope. Hence obviously the gel preparation fulfils the requirement of freedom from particular matter and from grittiness as desired for any topical preparation

Table no. 4

Formulation	Grittiness
F1	Not found
F2	Not found
F3	Not found
F4	Not found
F5	Not found
F6	Not found

3. Determination of pH

The pH of various gel formulations was determined by using digital pH meter. One gram of gel was dissolved in 100 ml distilled water and stored for two hours. The measurement

of pH of each formulation was done in triplicate and average values are calculated.

Table no. 5

Formulation	pH
F1	6.70 ±0.2
F2	6.68±0.1
F3	6.71±0.1
F4	6.77±0.2
F5	6.70±0.1
F6	6.77±0.3

4. Drug Content

1 g of the prepared gel was mixed with 100ml of phosphate buffer. Aliquots of different concentration were prepared by suitable dilutions after filtering the stock solution and absorbance was measured. Drug content was calculated using the equation, which was obtained by linear regression analysis of calibration curve

Table no. 6

Formulation	Drug Content
F1	90.28%±1.3
F2	90.65%±1.7
F3	92.04±1.5
F4	90.34±1.1
F5	91.33±1.2
F6	91.89±1.9

5. Viscosity, appearance, gelling, determination

The measurement of viscosity of the prepared gel was done with a Brookfield Viscometer. The gels were rotated at 0.3, 0.6 and 1.5 rotations per minute. At each speed, the corresponding dial reading was noted. The viscosity of the gel was obtained by multiplication of the dial reading with factor given in the Brookfield Viscometer catalogues3.

Table no. 7

Formulation	Viscosity (CPS)	Appearance	Gelling
F1	14420±75.68	Translucent	+
F2	15330±86.34	Translucent	+
F3	15261±87.65	Translucent	+++
F4	15427±54.76	Translucent	++
F5	15734±67.45	Translucent	++
F6	15856±43.35	Translucent	++

RESULTS AND DISCUSSION

Various observations and calculations were done for optimized formulations on different evaluation parameters such as viscosity, pH, homogeneity, grittiness and feel on application, drug content and drug diffusion.

Homogeneity was observed on visual basis which showed good homogeneity in F3 and free from any lumps and aggregation.

No appreciable particulate matter was seen under light microscope. No foreign particulate particles observed and the gel was smoothly applicable. The topical preparation was found to possess the grittiness as required for the topical gel.

The pH of gel formulation was determined by the digital pH meter. The pH was found to be 6.71 which are within the acceptable limit for topical formulations.

The viscosity range of the F3 gel formulation was 15261 cps which is within acceptable range for topical formulations.

The drug content in the formulation F3 was determined 92.04%.

Drug diffusion studies were carried out by using a cellophane membrane. The cumulative present drug release was found to be 99.33% in 3 hours.

At the end the release kinetics of the optimized gel was studies on the basis of different models suggested for release kinetics such as zero order model, first order model, Higuchi model and Krosmeyer- Peppas model. The values of regression coefficient was found to be R^2=0.986 for zero order model, R^2=0.985 for first order model, R^2=0.983 for Krosmeyer-peppas model, R^2=0.945 for Higuchi model. On the basis of data obtained, the optimized formulation was found to possess the release pattern of zero order models that shows the drug release pattern is sustained release.

CONCLUSION

It can be concluded that naproxen gel containing sandalwood oil can be an effective drug delivery system in the treatment of rheumatoid arthritis since it relives the side effects of naproxen. Therefore the present topical drug delivery system can be a useful alternative to the currently available marketed preparation i.e. Xenobiod Gel.

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