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RESEARCH ARTICLE

Design And Characterisation Of Ibuprofen Transemulgel.

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ABSTRACT

The goal of present project was to study the possibility of trans dermal application of ibuprofen with emulgel formulations. Ibuprofen (NSAIDs) is hydrophobic in nature it is insoluble in water. This limitation was overcome by preparing in the form of emulgel. Ibuprofen Emulgel formulations were developed by using 3 types gelling agents: carbopol 934, carbopol 940 and NaCMC. Ibuprofen emulgel formulations were assessed for different parameters such as physical appearance and pH values, Swelling index, Spreadability, Extrudibility, Drug content. In-vitro drug release study. All developed emulgel formulations exhibited suitable physical properties relating to colour, homogeneity and consistency. pH values of emulgels were seen in the scope of 5.98 to 6.51. Swelling index of all formulations was seen in the scope of 132% to 296%. Spreadability of all emulgel formulations was seen in the scope of 4.0 to 6.3. Extrudability of all emulgel formulations was seen in the scope of 2.34 to 18.5. Drug content of entire emulgel formulations ranged between 73.2% to 112.6%. In- vitro drug release studies showed 69.04% to 99.52% release towards the finish of 6 hours. The eventual objective of this drug delivery framework is to augment therapeutic activity while limiting the negative reactions of the drug. In such manner emulgel is helps to transfer the ibuprofen drug through the transdermal drug delivery system.

Keywords: Ibuprofen, Emulgel, Gelling agents, Transdermal, Parameters.

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INTRODUCTION

Ibuprofen is most commonly used nonsteroidal Anti-inflammatory drug with anti-inflammatory, analgesic and antipyretic effect. Like other NSAIDs, the normal side effect of ibuprofen in oral dosage form is upset stomach, nausea, vomiting, headache, diarrhoea, constipation, dizziness or drowsiness may occur [1]. Thus, other routes of administration for these drugs are being currently investigated. Recently, more concentration has been focused on emulgel for transdermal drug delivery wherein the gel and emulsion are used in combined form, the dosage form are denoted to as emulgel. Emulgel is prepared both Oil in water (O/W), and water in Oil (W/O) type emulsion mixed with gel. Oil in water type is used for lipophilic drugs and water in oil type is used for hydrophobic drug s' delivery [2].

The system is failed in the administration of hydrophobic drug. This limitation is over come by developing emulgel. The emulsion and gel preparations have their own properties. But the gels show some limitations is overcoming by emulgel. By the use of gelling agent classical emulsion can be converted into emulgel. The emulgel have many advantages like greaseless, thixotropic, easily spreadable, easily removable.

The main aim of transdermal drug delivery system is to transport drugs into systemic circulation through skin at predetermined rate with minimum inter and intra patient variation. Presently transdermal delivery is one of the most hopeful methods for drug application. It decreases the load that the oral route normally places on the digestive tract and liver. It enhances patient compliances and reduces harmful side effects of a drug caused from temporary overdoses [3,4].

Our present research work was carried out to investigate the possibility of transdermal application of ibuprofen emulgel formulations. Furthermore, the effect of gelling agent concentration, emulsifying agent concentration and oil phase concentration on swelling index, spreadability, extrudability and drug release also was investigated.

MATERIALS AND METHODS

Ibuprofen was purchased from Yarrow chemical products, Mumbai, India. Carbopol934 was purchased from Yarrow chemical products, Mumbai, India. Carbopol940 was purchased from Rolex chemical industries, Mumbai, India. NaCMC was purchased from Merck specialties pvt. Ltd, Mumbai, India. Tween 80 was purchased from RFCL Ltd, New Delhi, india. Span 80 was purchased from pallav chemicals and solutions pvt. Ltd, Boisar, India. Propylene glycol was purchased from karnataka fine chemicals, Bangalore, India. Liquid paraffin and Triethanolamine were purchased from Finar Ltd, Ahmedabad, Gujarat, India. Propyl paraben and Methyl paraben was purchased from pallav chemicals and solvents pvt.Ltd, Boisar, India. All other chemicals and ingredients used were of analytical grade [5-6].

Construction of calibration curve of ibuprofen

Determination of λ max

The standard solution of ibuprofen (20µg/ml) was scanned in the wavelength region of 200-400nm and the λ max found to be as 224nm.

Preparation of calibration curve at 224nm

The working standard solutions of ibuprofen were scanned in the UV region and absorbance were observed against phosphate buffer (pH-5.5) as a blank at 224nm. Finally, the calibration curve was plotted between concentration (x-axis) and absorbance (y-axis). (depicted in Table 1 and Figure 1)

Preparation of Ibuprofen emulgel

Extraction of Aloe vera gel

- The central parenchymatous pulp was scooped out with a spatula from the ALOE leaves and the pulp was washed repeatedly with water and finally treated through 0.1 N sodium hydroxide to avoid the acidity in preparation.

- The treated pulp was put down in blender to gain the juice.
- The obtained juice was exposed to filtration.
- To the pure liquid so obtained, 0.5%N NaOH solution was added drop wise and stored in air tight containers in a dark room to prevent photo-oxidation [7-8].

Step 1: Preparation of emulsion either o/w or w/o.

Step 2: Preparation of gel base.

Step 3: Incorporation of emulsion into gel base with continuous stirring.

Step-1:

- The oil phase of emulsion was prepared by dissolving span 80 in liquid paraffin while the aqueous phase was prepared by dissolving tween 80 in purified water.
- Methyl and propyl parabens were dissolved in propylene glycol where as IBUPROFEN was dissolved in ethanol, and both solutions were mixed to aqueous phase.
- Both the oily and aqueous phases were individually heated to 70°-80°C then the oily phase was added to the aqueous phase with continuous stirring until cooled to room temperature.

Step-2:

- In the preparation of emulgel first we go for the preparation of gel base, carbopol 934 is the commonly used gel formers and at low concentration it forms good consistency transparent gel. It will be prepared by dispersing carbopol 934 in distilled water.
- While dispersing carbopol into distilled water, aloe vera gel and clove oil are also added and soak it for 24hrs.
- The same procedure is followed for the preparation of gel bases i.e., carbopol940 and sodium CMC.
- *Step-3:*
- The gained emulsion was mixed with the gel base in 1:1 ratio with gentle stirring to obtain the emulgel.
- Finally pH of emulgel was adjusted by using triethanolamine[9-10].

Evaluation of ibuprofen emulgel

Physical examination

The prepared emulgel formulations were inspected visually for their colour, homogeneity, consistency, grittiness and separation.

Measurement of pH

The pH values of emulgel formulations were determined by using digital pH meter. 1gm of emulgel was dissolved in 100ml of distilled water and stored for two hours. The measurement of pH of each formulation was done in triplicate and average values were calculated [11].

Swelling index

It is determined by taking 1g of emulgel in a porous aluminium foil and mixed with 0.1N NaOH kept in a 50ml beaker. These samples are withdrawn at different time intervals and kept for drying and it is reweighed. It is calculated as follows:

$$\text{swelling index} = \{Wt - Wo/Wo\}100$$

where, (SW) %= Equlibrium percent swelling,
Wt = Weight of swollen emulgel after time "t" Wo= Weight of emulgel at zero time.

Spreadability

- It is measured in terms of diameter of emulgel circle produced when prepared emulgel is placed between 2 glass plate of definite weight.
- Weighed quantity (350mg) of prepared emulgel is taken on one glass plate and another glass plate is dropped from a distance of 5cm.
- Diameter of circle of spread emulgel is measured [12-13].

Extrudibility study

It is calculated by the power required to extrude the prepared emulgel from the tube. The method applied for determination of applied shear in the region of the rheogram corresponding to a shear rate exceeding the yield value and showing consequent plug flow. In this study prepared emulgel extruded from lacquered aluminium collapsible tube on application of weight in grams required to extrude at least 0.5 cm ribbon of emulgel in 10 seconds. For better extrudability, more quantity is extruded. For the measurement of extrudability, it is done in triplicate and the average values are calculated. The Extrudability is calculated by using the following formula:

Extrudibility = Weight applied to extrude emulgel from tube (in gm)/ Area (in cm2).

Drug Content

Emulgel is mixed in a suitable solvent. Filter it to get pure solution. Determine its absorbance using UV spectrophotometer. From the standard equation by putting the absorbance value concentration and drug content can be obtained.

Drug Content = (Concentration ×Dilution Factor ×Volume taken) ×Conversion Factor.

In-vitro Drug release Studies:

Franz diffusion cell is used for the study. Emulgel is applied on the surface of egg membrane is fixed between the donor & the receptor chamber of diffusion cell. The receptor chamber contains freshly prepared PBS (pH5.5) solution to solubilize the drug. The receptor chamber is stirred using magnetic stirrer. The samples (1.0ml aliquots) are collected at different time intervals and analyzed for drug content by uv-vis spectro photo meter after appropriate dilutions. Drug release is based on a function of time[14-16].

RESULTS AND DISCUSSION

Physical Examination

The prepared ibuprofen emulgel formulations were white, viscous, creamy preparation with smooth and homogeneous appearance.

pH measurement

The pH values of all prepared emulgel formulations were found to be 5.98 to 6.51. (showed in Table 3 and Figure 2)

Swelling index

In Ibuprofen emulgel formulations the swelling of fabricated hydrogels increases as the concentration of carbopo-934 and corbopol-940 composition increases. The increased is attributed to the higher concentration of the carboxylic groups in gelling agents that ionize more at a high PH and leads to repulsion among the same group charges, and as a result, swelling is increased.

But in case of NaCMC, swelling index is decreased with the increasing concentrations of NaCMC. The reduction is attributed to the fact that the network chains became inflexible at high density of NaCMC, thus smaller quantity of water molecules penetrates the hydrogel structure.

Hence, from the above discussion, it is clear that swelling index is greater for formulations possessing Carbopol 934 compared to Carbopol 940 and NACMC, and as the concentration of former increased, swelling index increased accordingly, in the order F1 < F2 <F3. The least swelling index values were observed with NaCMC, as the concentration of which increased, drastic decrease in the swelling capacity giving the values in the order F7 > F8 > F9.

Thus, in the above formulations, carbopol-934 formulations exhibited higher swelling index values than compare with carbopol-940 and NaCMC. Any variation in the swelling index value is dependent on the water uptake nature of the polymers. Swelling index of prepared ibuprofen emulgel formulations is shown in Table 3 and Figure 3.

Spreadability

In Ibuprofen emulgel formulations, with increasing concentrations of gelling agent (carbopol-934 and corbopol-940 and NaCMC), spredability was decreased gradually. In addition, viscosity increased as concentration of gelling agent increased. Thus, high concentration of gelling agents as well as increased viscosity is accountable for decreasing spreadability of the ibuprofen emulgel.

In case of carbopol-934, the spredability was in descending order i.e., F1 > F2 > F3. Here, spredability through F1 is high than F2 and F3 due to less viscous emulgel formation. Similarly, for carbopol-940 and NaCMC, the spredability was found to be in its descending order which was accountable to the increased gelling agent concentration.

Thus, in the above formulations, carbopol-934 formulations exhibited higher spreadability values than with carbopol-940 and NaCMC owing to its less complex gelling capacity and less viscose nature was observed with increasing concentrations of carbopol 934, 940 and NaCMC. The results are shown in Table 3 and Figure 4.

Extrudability

In Ibuprofen emulgel formulations, with increasing concentrations of gelling agent (carbopol-934 and corbopol-940 and NaCMC), consequently the viscosity of the gellified emulsion increased which leads to decrease in the extrudability of the ibuprofen emulgel. Thus high concentration of gelling agents as well as increased viscosity is accountable for decreasing the extrudability of the ibuprofen emulgel.

In case of carbopol-934, the extrudability of the ibuprofen emulgel was in descending order i.e., F1 > F2 > F3. Here, extrudability of the F1 is high than F2 and F3 due to less viscous emulgel formation. Similarly, for carbopol-940 and NaCMC, the extrudability was found to be in its descending order which was accountable to the increased gelling agent concentration.

Thus, in the above formulations, carbopol-934 formulations exhibited higher extrudability values than with carbopol-940 and NaCMC owing to its less viscosity and less complex gelling capacity was observed with increasing concentrations of carbopol 934, 940 and NaCMC. Extrudability of prepared ibuprofen emulgel formulations are presented in Table 3 and Figure 5.

Drug content

The percentage drug content of all prepared ibuprofen emulgel formulations was found to be 73.2-112.6%. Drug content of all prepared formulations is shown in table 3.

Invitro drug release study

In Ibuprofen emulgel formulations, with increasing concentrations of gelling agent (carbopol-934 and corbopol-940 and NaCMC), the diffusion of the drug through the membrane decreased gradually. In addition, viscosity increased as concentration of gelling agent increased. Thus, high concentration of gelling agents as well as increased viscosity is accountable for decreasing the release of active substance from the ibuprofen emulgel.

In case of carbopol-934, the cumulative amount of drug release was in descending order i.e., F1 > F2 > F3. Here, drug release through F1 is high than F2 and F3 due to less viscous emulgel formation. Similarly, for carbopol-940 and NaCMC, the drug release was found to be in its descending order which was accountable to the increased gelling agent concentration.

Thus, in the above formulations, carbopol-934 formulations exhibited higher drug release values than with carbopol-940 and NaCMC owing to its less complex gelling capacity. Sustained action was observed with increasing concentrations of carbopol 934, 940 and NaCMC.

In first hour of diffusion studies drug release was observed ranging from 2.095-27.91%, for all formulation. In-vitro drug release studies were performed over a period of 6hrs maintaining sink conditions. Percentage cumulative drug release were obtained as 99.52, 98.33, 96.26, 84.29, 81.59, 77.08, 79.33, 75.60, 69.04, respectively. The drug release was sustained with the increasing concentrations of gelling agent. The drug release profile data is presented in Figure 6 and 7.

Table-1: Calibration Curve data of Ibuprofen.

S.No	Concentration µg/ml	Absorbance (nm)
1	0	0
2	2	0.171
3	4	0.315
4	6	0.474
5	8	0.614
6	10	0.735

Table-2: Formulation of Ibuprofen emulgel

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Carbapol934	1	1.2	1.5	-	-	-	-	-	-
Carbapol940	-	-	-	0.5	1.0	1.5	-	-	-
NaCMC	-	-	-	-	-	-	5	5.5	6
Ibuprofen	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Span80	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Tween80	1	1	1	1	1	1	1	1	1
Liquid Paraffin	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Triethanolamine			Adjust	the	pH	from	5.5 to	6.5	
Propyl Paraben	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Methyl paraben	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Aloe vera (1%)	1	2	3	-	-	-	-	-	-
Purified Water	100	100	100	100	100	100	100	100	100
Clove Oil	-	-	-	7	7.5	8	-	-	-
Propylene glycol	5	5	5	5	5	5	5	5	5

Table-3: pH values, Swelling index, Spreadability, Extrudability, Drug content.

S.NO	Formulation code	pH values	Swelling index (%)	Spreadability (gm.cm/sec)	Extrudability (gm.cm/sec)	Drug content (%)
1	F1	5.98	246%	6.3	18.5	76.5%
2	F2	6.13	282%	5.4	9.36	79.8%
3	F3	6.32	296%	4.5	3.82	86.5%
4	F4	6.04	234 %	5.7	14.2	92.4%
5	F5	6.45	269%	5.2	8.42	89.9%
6	F6	6.06	282 %	4.2	2.73	76.5%
7	F7	6.51	185%	5.6	12.02	73.2%
8	F8	6.24	154 %	4.8	7.31	80.4%
9	F9	6.31	132 %	4.0	2.34	112.6%

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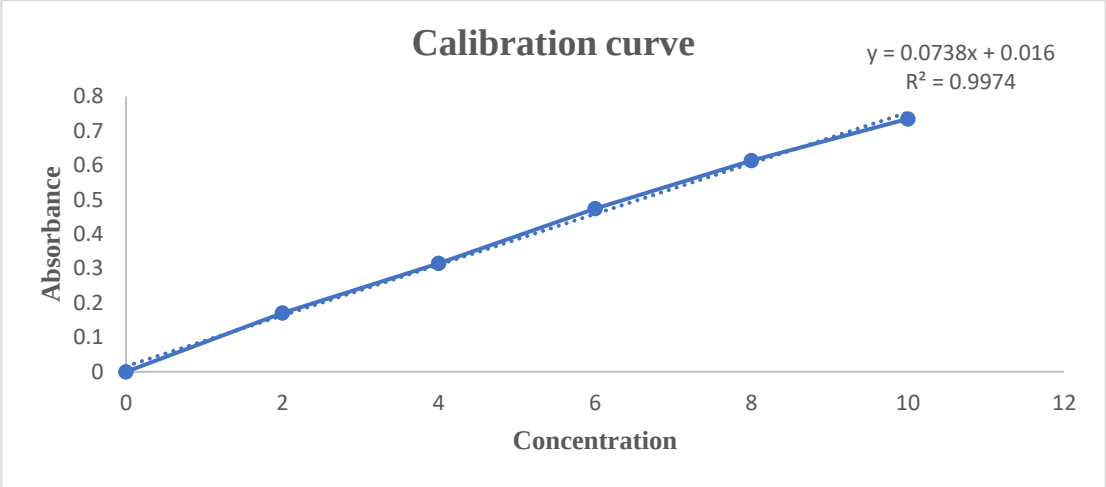

Figure 1: Calibration Curve of Ibuprofen

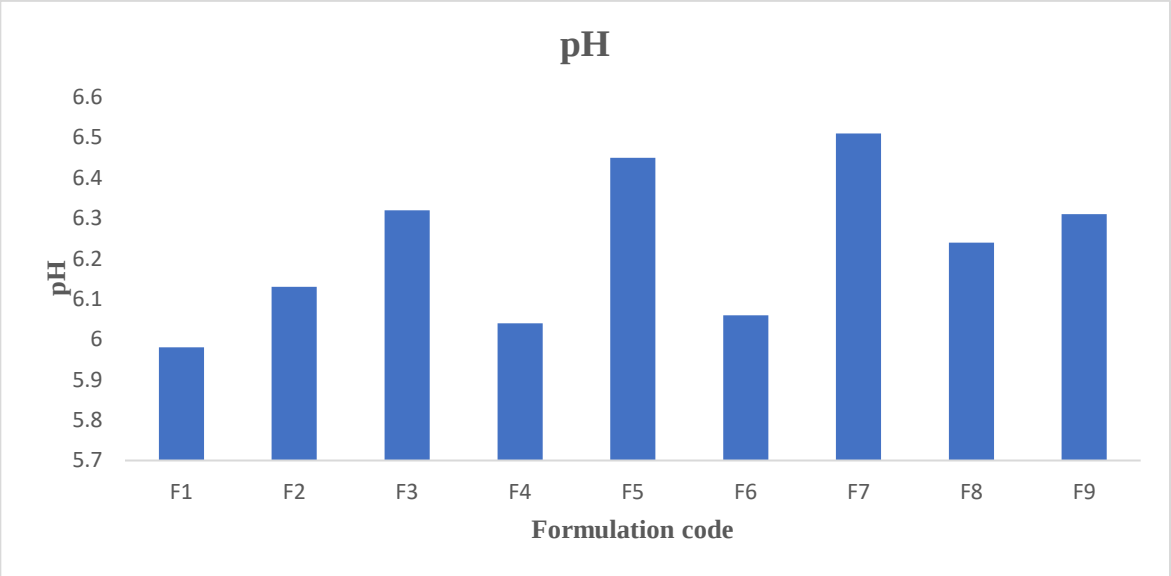

Figure 2 : Bar graph of pH values

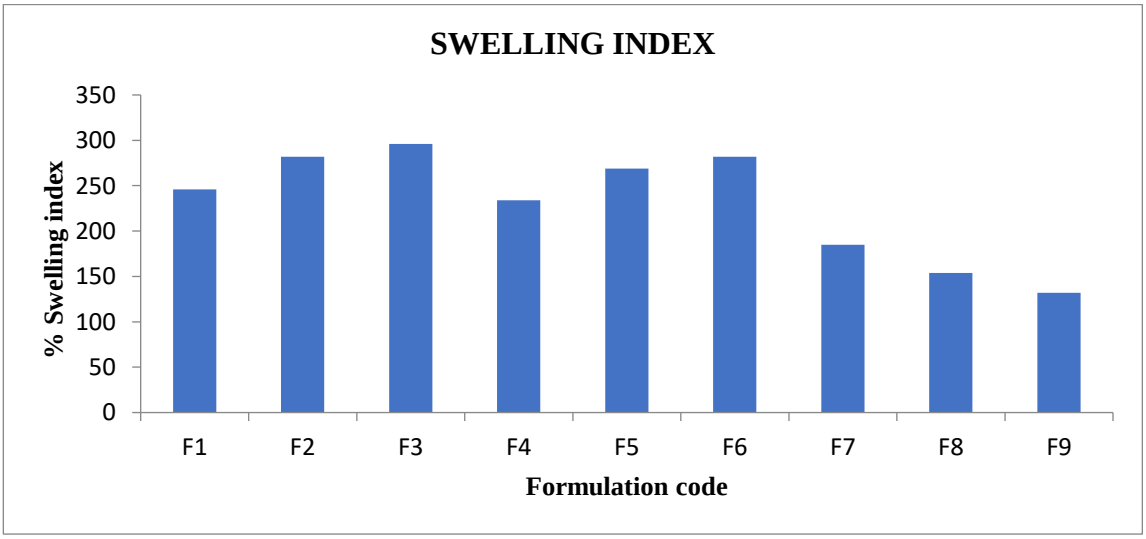

Figure 3: Bar graph of Swelling index values

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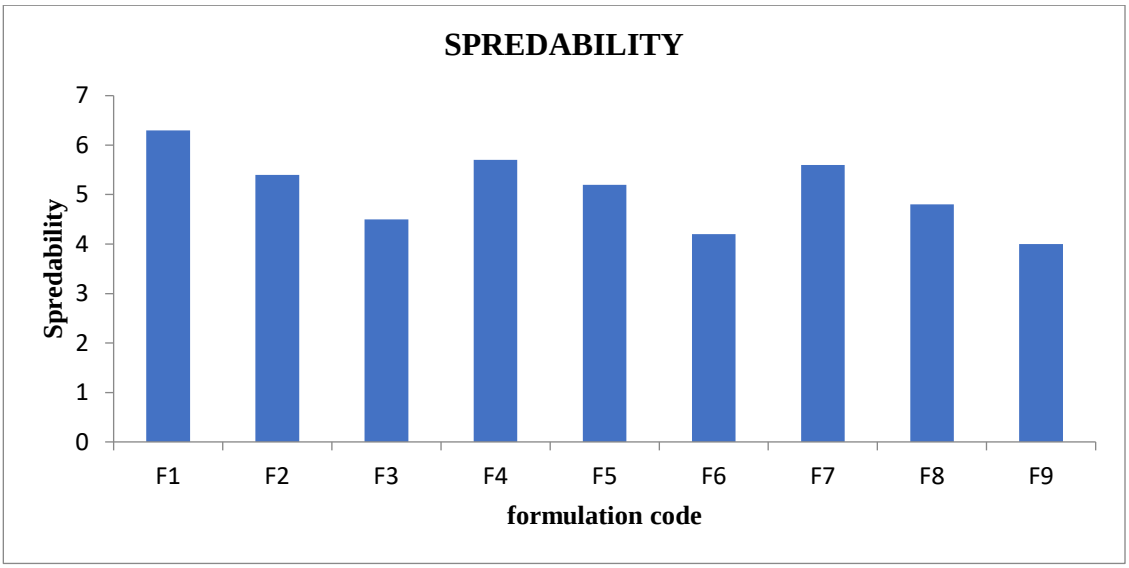

Figure 4: Bar graph of Spreadability values

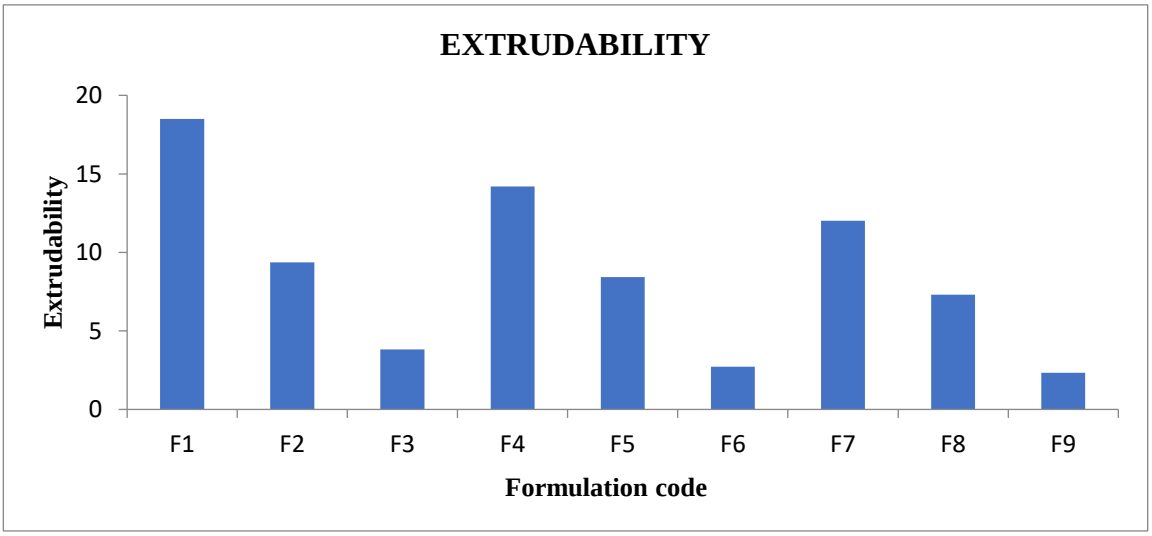

Figure 5: Bar graph of Extrudability values

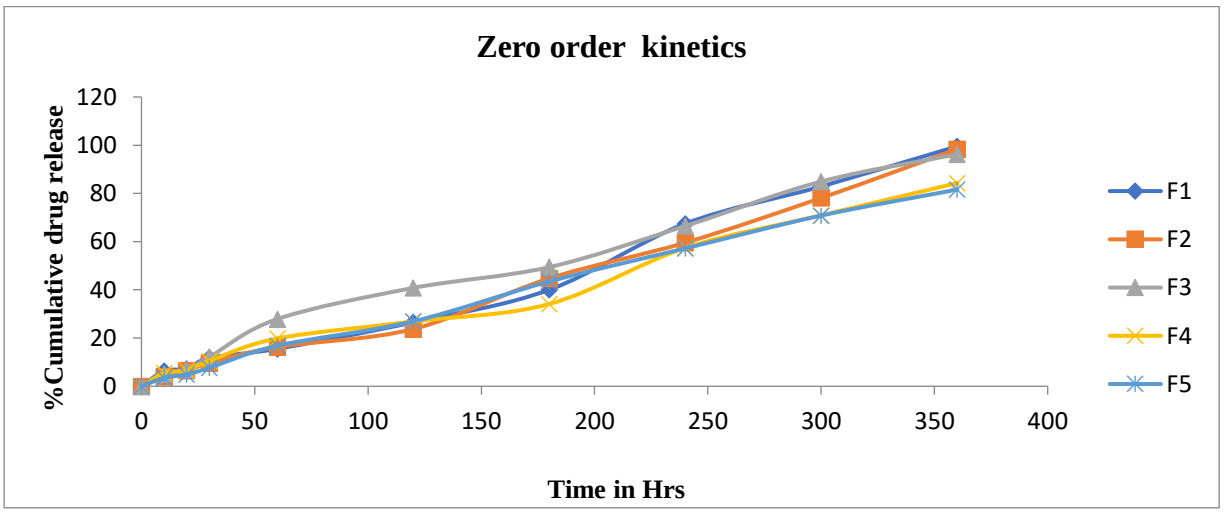

Figure 6: In-vitro drug release studies for formulation F_1 to F_5

Figure 7: In-vitro drug release studies for formulation F_6 to F_9

CONCLUSION

The study was aimed to prepare emulgel of ibuprofen to investigate the possibility of trans dermal application. Emulgel formulations of ibuprofen were developed by using carbopol 934, carbopol 940 and NaCMC as gelling agents, span 80 and tween 80 as emulsifiers and liquid paraffin as oil phase, and aloe Vera, clove as permeation enhancers. Prepared emulgel were evaluated for their physical appearance and pH values, swelling index, Spreadability, extrudability, drug content. In-vitro drug release study. As a general conclusion all the formulations exhibited good In-vitro drug release indicating the sustained release of drug.

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