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TOPICAL DELIVERY OF SUMATRIPTAN EMULGEL: DESIGN, DEVELOPMENT, IN VITRO, EX VIVO CHARACTERIZATION AND IN VITRO-EX VIVO CORRELATION

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Abstract:

Emulgels have emerged as a promising drug delivery system for the delivery of hydrophobic drugs. The objective of the study was to prepare emulgel of, using Carbopol 940P as a gelling agent which has good viscosity which makes them fairly popular for controlling the flow properties of topically applied dosage forms as they are inexpensive, transparent, harmless, easy to wash and prepare and clove oil were used as penetration enhancers The emulsion was prepared and it was incorporated in gel base. The formulations were evaluated for rheological studies, spreading coefficient studies, in vitro release, ex vivo release studies. Developed emulgel formulations possessed the required physicochemical properties such as good physical appearance, drug content uniformity, excellent spreadability and extrudability. F4 were subjected to stability studies which showed satisfactory results. Stability study of the formulation showed no significant changes in the drug content as well as physical characteristics. The formulation (F4) has fulfilled the objectives of the present study like increasing the bioavailability, reduction in the frequency of administration, improved patient compliance

Key words: *Emulgel, Transparent, Carbopol 940P, spreadability, extrudability,*

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INTRODUCTION:

Topical drug delivery can be defined as the delivery of drug to the skin directly and reaches the systemic circulation at sufficient concentration to ensure the therapeutic efficacy. The main advantage of the topical delivery system is it bypasses the first pass metabolism and gastric degradation [1-3]. Avoidance of the risks and inconveniences associated of intravenous therapy and of the varied conditions of absorption, like pH changes, the presence of enzymes, gastric emptying time [1].

Many widely used topical agents like ointments, Creams lotions have many disadvantages. They are sticky in nature causing uneasiness to the patient when applied, have lesser spreading coefficient so applied by rubbing and they also exhibit the problem of stability. Due to all these factors within the major group of semisolid preparations, the use of transparent gels has expanded both in cosmetics and in pharmaceutical preparations. Gels for dermatological use have several favourable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, compatible with several excipients, and water-soluble or miscible. In spite of many advantages of gels a major limitation is in the delivery of hydrophobic drugs. So to overcome this limitation an emulsion based approach is being used so that even a hydrophobic therapeutic moiety can be successfully incorporated and delivered through gels[4-5].

Emulgels are emulsions, either of the oil-in-water or water in- oil type, which are gelled by mixing with a gelling agent. They have a high patient acceptability since they possess the previously mentioned advantages of both emulsions and gels. Emulgel for dermatological use have several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, water soluble, longer shelf life, bio friendly, transparent and pleasing appearance. Therefore, they have been recently used as vehicles to deliver various drugs to the skin[6].

Transdermal therapeutic systems have been designed to provide controlled continuous delivery of drugs via the skin
to the systemic circulation [3-4] Moreover, it over comes various side effects like painful delivery of the drugs and the first pass metabolism of the drug occurred by other means of drug delivery systems [5].

Sumatriptan is a serotonin receptor agonist commonly used to treat migraines and acute cluster headaches. It is one of the more commonly prescribed migraine therapies [7]. The aim of the present investigation study is to develop emulgel of for topical administration. The main clinical benefits of emulgels are their ability to improve bioavailability and patient compliance by avoiding first pass metabolism and GIT degradation [8].

Daily dose of sumatriptan is 50 mg or less is preferable. Hence, it can be conveniently formulated. Molecular weight of drug is 295.4 g/mol. So the drug gets easily absorbed through skin. Oral administration of this drug has lower absorption of about 15% only because it undergoes extensive first pass metabolism by the cytochrome P450 isoenzymes, so its bioavailability may be significantly improved if delivered through topical route. Its biological half-life is 2.5hrs will be good candidates for topical drug delivery system. These reasons were considered as potential route to formulate topical delivery system, which can improve its bioavailability by avoiding hepatic metabolism.

MATERIALS:

The pure drug sumatriptan was obtained from KP Labs, Hyderabad, India. Carbopol 940P and Liquid paraffin were purchased from Central Scientific Supplies Co Ltd., Hyderabad, India. Span 20 and Tween 80 was procured from Rezon Scientifics, Hyderabad, India. Ethanol, Clove oil and Propylene glycol were obtained from Vijay Enterprises, Hyderabad, India. Methyl paraben, Propyl paraben was obtained Central scientific supplies Co Ltd, Hyderabad, India. Sodium hydroxide, Potassium di-hydrogen orthophosphate and Hydrochloric acid were procured from U V Scientifics, Hyderabad.

MEHODS:

Preformulation studies of the selected drug:

Solubility determination:

The solubility of the selected drug was determined in distilled water and phosphate buffer of pH 7.4 using standard method [9].

Procedure:

Excess amount of the selected drug was taken and dissolved in a measured amount of above solvents separately in a glass beaker to get a saturated solution. The solution was shaken intermittently to assist the attainment of equilibrium with the undissolved drug particles. Then measured quantity of the filtered drug solution was withdrawn after 24hrs and successively diluted with respective solvents and the concentration was measured spectrophotometrically. Average of triplicate readings was taken.

Melting point determination:
Melting point of the drug was determined by taking a small amount of the drug in a capillary tube closed at one end and was placed in Thiel's melting point apparatus and the temperature at which the drug melts was noted [8,10]. Average of triplicate readings was taken.

Partition coefficient determination:
A drug solution of 1mg/ml was prepared in n-octanol, 25ml of this solution was taken in a separating funnel and shaken with an equal volume of phosphate buffer of pH 7.4 (aqueous phase) for 10 minutes and allowed to stand for two hrs. Then aqueous phase 50 and organic phase were collected separately and centrifuged at 2000 rpm. Both the phases were analyzed for the drug concentration using UV-spectrophotometer. Partition coefficient was calculated by taking the ratio of the drug concentration in n-octanol to drug concentration in aqueous phase [10-11].

Permeability coefficient determination:
The permeability coefficient of drug was calculated by "Potts and Guy equation"[8,11],

$$\text{Log Kp} = -2.7 + 0.71 \times \log \text{Ko/w} - 0.0061 \times \text{Molecular weight}$$

Where,

Log Kp = Permeability coefficient
Ko/w = Partition coefficient

Preparation of Standard graph of sumatriptan in pH 7.4 phosphate buffer by UV-Visible Spectrophotometer:
The stock solution was freshly prepared by dissolving 100mg of sumatriptan in 7.4 pH phosphate buffer in a 100ml volumetric flask and then making up the solution up to the mark using 7.4 pH phosphate buffer for obtaining the solution of strength 1000µg/ml (stock I). From this primary stock 10ml of this solution is diluted to 100ml with distilled water to obtain a solution of strength 100µg/ml (stock II). From this secondary stock 0.4, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8ml were taken separately and made up to 10ml with pH 7.4 phosphate buffer, to produce 4, 8, 10, 12, 14, 16, 18µg/ml respectively. The absorbance was measured at 249nm using a UV-Visible spectrophotometer.

Drug excipients compatibility studies:
Fourier Transform Infrared (FTIR) Spectroscopy:
The Fourier transform infrared (FTIR) spectra for the samples were obtained using KBr disk method by FTIR spectrophotometer [12]. Pure drug sumatriptan, Physical mixture of sumatriptan and Carbopol 940P, Physical mixture of sumatriptan and liquid paraffin were prepared and subjected to FTIR study. About 2–3 mg of sample was mixed with dried potassium bromide of equal weight and compressed to form a KBr disk. The samples were scanned from 400 to 4000 cm^{-1} spectral region with a resolution of 4 cm^{-1}.

Formulation Development:
The emulgels were prepared by modified conventional method of preparation [13-14]. This method is described as follows:

Emulsion preparation:
The oil phase of the emulsion was prepared by dissolving span 80 and methyl paraben in measured quantity of light liquid paraffin. At last, add measured quantity of clove oil. The aqueous phase was prepared by dissolving Tween 80 in propylene glycol whereas sumatriptan drug was dissolved in ethanol. The prepared drug solution has been thoroughly mixed with the glycol solution; at the same time propyl paraben was also being dissolved and the measured quantity of water was added. Both the phases were separately heated up to 40° to 50°C in the water bath, then the oil phase was added to aqueous phase with continuous stirring and cool it to room temperature.

Gel preparation:
The Gel in the formulations were prepared by slowly dispersing accurately weighed quantity of Carbopol 940P polymer pinch by pinch in purified water with constant stirring at a moderate speed and kept it stirred for 10 minutes.

Emulgel preparation:
Add gel solution drop by drop in emulsion with constant stirring at moderate speed then the pH has been adjusted to 6–6.8 using Tri Ethanol Amine (TEA). Continued stirring up to 5 minutes resulted into formation of emulgel with better consistency.

Table 1: Formulation of Sumatriptan Emulgel (Ingredients in %w/v)

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
Sumatriptan	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
Carbopol 940P	0.5	1	1.5	1.75	2	2.5	2.75	3
Liquid Paraffin	5	5	5	5	5	5	5	5
Span 20	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Tween 80	1	1	1	1	1	1	1	1
Propylene glycol	2	2.5	3	3.5	4	5	6	7
Ethanol	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Clove Oil	3	3	3	3	3	3	3	3
Methyl Paraben	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Propyl paraben	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Water (q.s)	40	40	40	40	40	40	40	40

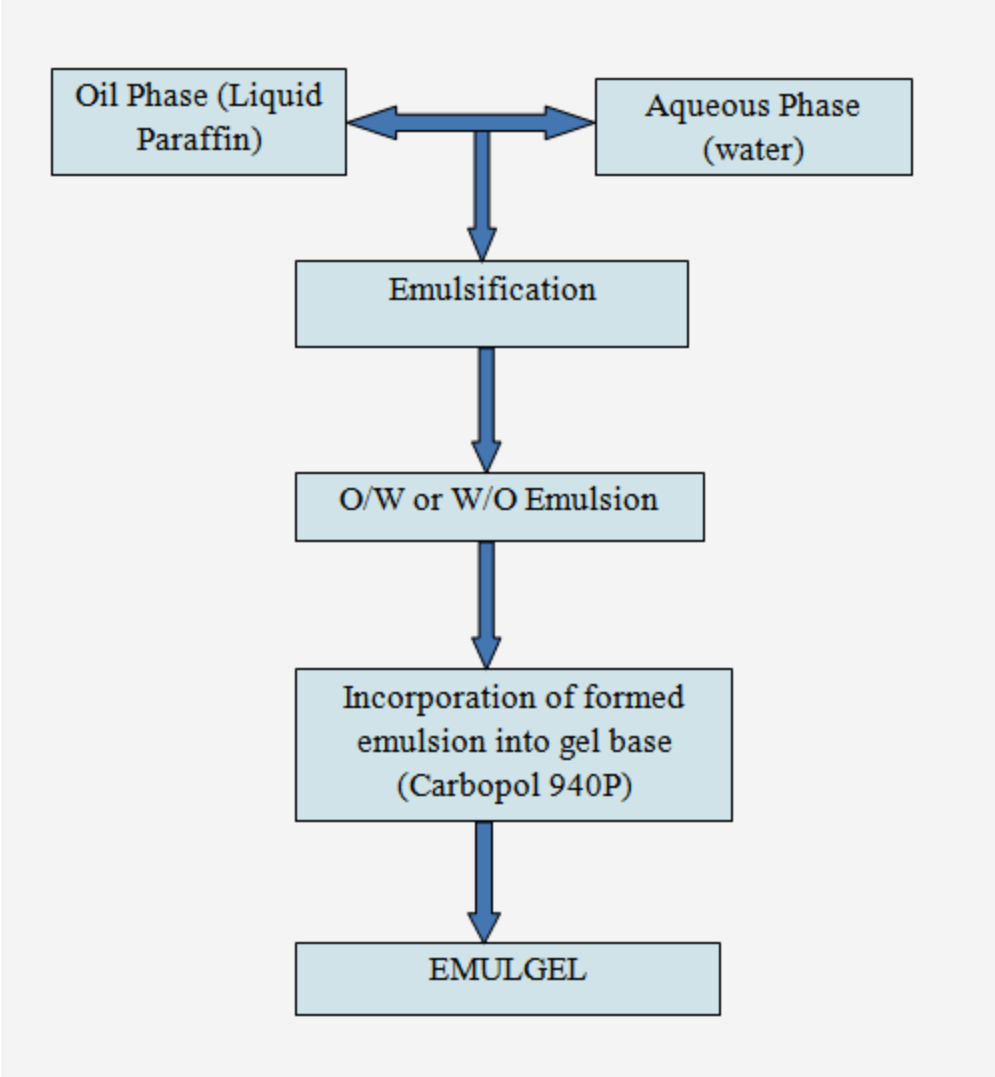

Figure 1: Method of formulation of emulgel

Characterization of emulgel[14-15]

Physical appearance:

The prepared emulgel formulations are inspected visually for their color, homogeneity, consistency and phase separation after 24 h of preparation.

pH:

The pH values of 1% aqueous solutions of the prepared emulgels were measured by a calibrated pH meter.

Spreadability:

The spreadability of the emulgel formulations was determined 48 hrs after preparation, by measuring the spreading diameter of 0.5 g emulgel which was placed within a circle of 1 cm diameter pre-marked on a glass plate over which a second glass plate (75 gm) was placed. A weight of 425 g was allowed to rest on the upper glass plate for 5 min where no more spreading was expected. The increase in the diameter due to spreading of the gels was noted. The spreadability (g.cm.min-1) was calculated by using the formula:

$$S = \frac{m\ X\ l}{t}$$

Where;

S is spreadability, m is the weight of the upper plate and rested on it (g),

l is the diameter of the spreading emulgel (cm), and

t is the time taken (min)[16].

Centrifugation:

This parameter could be measured to evaluate physical stability. Emulgel could be centrifuged at an ambient temperature and 6000 rpm for 10 minutes to evaluate the system for creaming or phase separation. System could be observed visually for appearance.

Extrudability
The various emulgel formulations were filled into closed collapsible tubes after formulating them and gel was pressed firmly at the crimped end and a clamp was applied to prevent any roll back. The cap was removed and the gel was extruded. The amount of the extruded gel was collected and weighed. The percentage of the extruded gel was calculated.

Rheological study [17]
The viscosity of various formulated batches was determined using a Brookfield viscometer (DV-E Viscometer) with spindle 64. Gels were filled in jar and spindle was lowered perpendicularly taking care that spindle does not touch the bottom of the jar and spindle was rotated in the gel at 20 rpm. The assembly was connected to a thermostatically controlled circulating water bath which was maintained at 25 °C. Spindle was allowed to move freely into the emulgel formulation and the reading was noted. At each speed, the corresponding dial reading was noted. The reverse reading was also noted and average was taken for these two readings. The viscosity of the gel was obtained by the multiplication of the dial readings with the factors given in the Brookfield viscometer catalogs.

Drug Content Determination
Take 1gm of emulgel. Mix it in suitable solvent. Filter it to obtain a clear solution. Determine its absorbance using UV spectrophotometer. Standard plot of drugs is prepared in the same solvent. Concentration and drug content can be determined by using the same standard plot by utilizing the value of absorbance.

***In-vitro* drug release study**
In-vitro release study is carried out using a modified Franz diffusion cell. 1g of the formulation was weighed and placed on the dialysis membrane having the surface area of 2.5cm^2, which is placed between the donor and receptor compartment of the diffusion cell. Phosphate buffer 7.4 was prepared and used as the diffusion media. The temperature of the cell was maintained at 37˚C. This whole setup was stirred using the Teflon coated magnetic stirrer at 50 rpm. At specified time intervals 5ml of the sample solution was taken and analysed spectrophotometrically at 249nm upto 4 hrs. The cumulative % drug release was determined.

Kinetic Analysis of *in-vitro* Release Rates of sumatriptan Emulgel
An appropriate drug release test is required to characterize the drug product and ensure batch to batch reproducibility and consistent pharmacological/biological activity and to evaluate scale up and post approval changes such as manufacturing site changes, component and composition changes. The release of drug from a sustained release formulation is controlled by various factors through different mechanism such as diffusion, erosion or osmosis. Several mathematical models are proposed by many researchers to describe the drug release profiles from various systems. In order to characterize the kinetics of drug release from dosage forms several model dependent methods are reported by various researchers. The model dependent methods all rely upon a curve fitting procedure. Different mathematical functions have been used to model the observed data. Both the linear and non-linear models are being used in practice for dissolution modeling. Linear models include Zero order, Higuchi, Hixson - Crowell, Quadratic and Polynomials, whereas the nonlinear models include First order, Weibull, Korsmeyer - Peppas, Logistic etc.

There are several linear and non-linear kinetic models to describe release mechanisms and to compare test and reference dissolution profiles are as follows [18]:

- Zero order kinetics
- First order kinetics
- Korsmeyer-Peppas model
- Higuchi model

The results of in vitro release profile obtained for all the formulations were plotted in modes of data treatment as follows,

1. Zero order kinetic model – Cumulative % drug released versus T.
2. First order kinetic model – Log cumulative percent drug remaining versus T.
3. Higuchi's model – Cumulative percent drug released versus square root of T.
4. Korsmeyer equation / Peppa's model – Log cumulative percent drug released versus log T.

Ex-vivo* release study*:
The *ex-vivo* drug release study of selected formulations was carried out in a modified Franz diffusion cell, using rat skin [12]. A section of skin was cut and placed in the space between the donor and receptor compartment of the Franz Diffusion cell, keeping the dorsal side upward. Phosphate buffer pH 7.4 was used as dissolution media. The temperature of the cell was maintained constant at 32 °C by circulating water jacket. This whole assembly was kept on a magnetic stirrer and the solution was stirred continuously using a magnetic bead. The samples (2ml) were withdrawn at suitable time intervals and

replaced with equal amounts of fresh dissolution media.

***In vitro ex vivo* correlation between cumulative % drug released *in vitro* and %drug release *ex vivo* of optimized formulation of emulgel (F4)**

In-vitro and *ex-vivo* correlation was carried out for the therapeutic efficacy of a pharmaceutical formulation. It was governed by the factors related to both *in-vitro* and *ex-vivo* characteristics of the drug. Percent *ex vivo* release on x-axis was plotted against *in vitro* drug release on y-axis for the same period of time [19]

Stability studies

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light and to establish a re-test period for the drug substance or a shelf life for the drug product and recommended storage conditions [20]

Stability studies were carried for most satisfactory formulation. The most satisfactory formulation stored and sealed in aluminum foil. These were stored at room temperature for 2 months and then evaluated for physical appearance, pH, rheological properties and drug content.

RESULTS AND DISCUSSION:

Preformulation studies:

Solubility, partition coefficient and Log P determination

In the first phase of our study the drug was subjected to various preformulation parameters namely solubility, melting point, partition coefficient (aqueous & octanol), permeability coefficient. The results were shown in table 6-7. The solubility of drug in water and phosphate buffer of pH 7.4 was found to be 0.578 mg/ml, 0.637 mg/ml respectively and partition coefficient and permeability coefficients were found to be 51.42 mg/ml, 32.78 mg/ml and 0.69 respectively.

Determination of melting point

The small amount of Sumatriptan drug was taken in a capillary tube and was placed in Thiel's melting point apparatus and the temperature at which the drug melts was noted. The average melting point of Sumatriptan drug was found to be 165.5˚C

Table 2: Preformulation studies of sumatriptan

S. No	Drug	Solubility(mg/ml)		Partition coefficient (P)		Log P	Melting point
		Water	Buffer pH 6.8	Amount in aqueous phase (mg/ml)	Amount in octanol (mg/ml)		
1	Sumatriptan	0.578	0.637	51.42	32.78	0.69	165.5˚C

Preparation of standard graph of sumatriptan in pH 7.4 phosphate buffer

Different concentrations were prepared in phosphate buffer 7.4 and absorbance values at λ_{max} (249 nm) were noted. The calibration curves showed a good linearity with correlation coefficient of R^2 0.999.

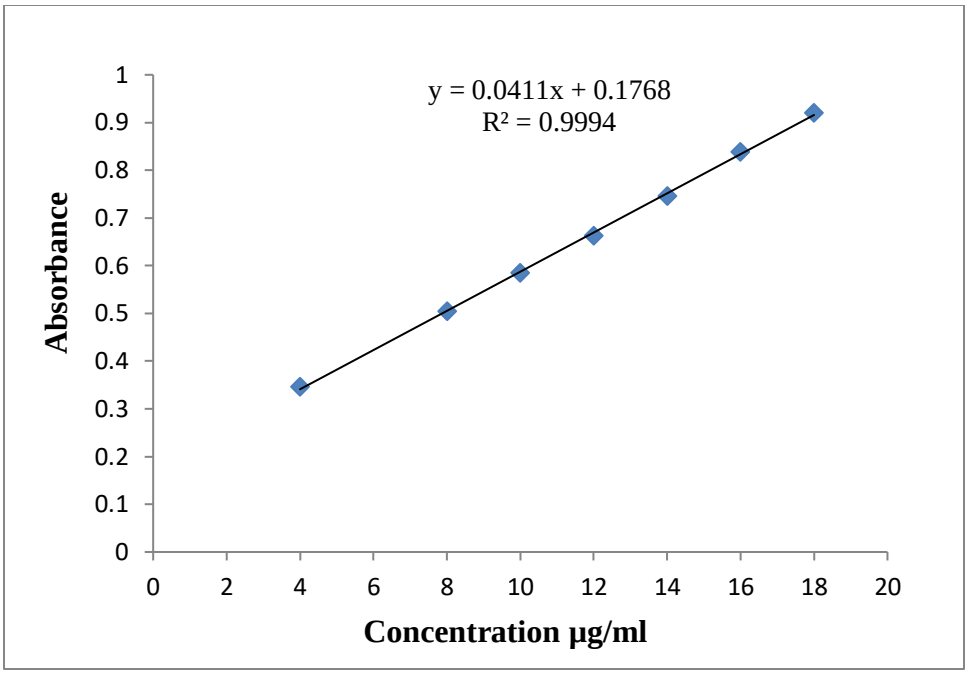

Figure 2: Standard graph of sumatriptan in pH 7.4 phosphate buffer

Drug-excipient compatibility studies:

Fourier Transform Infrared (FTIR) Spectroscopy studies:

Potential chemical interaction between drug and polymer may change the therapeutic efficacy of the drug. To investigate the possibility of any chemical interaction between drug and polymers used in the preparation of emulgels FTIR spectroscopic studies were carried out; samples were analyzed over the range 400–4000 cm^{-1}. The FTIR spectra of pure sumatriptan and polymers were given in Figure 3-5 respectively. The FTIR spectrum of sumatriptan demonstrates sharp transmittance bands for (C-H) at 2810 cm^{-1}, which also appears in the final spectrum. FTIR spectroscopic analysis of sumatriptan alone and in formulation showed presence of following peaks substantive of sumatriptan, namely C–H stretching and bending – 1434.96, 833.32, 879.19 cm^{-1} C–N stretching and bending – 1301.90 cm^{-1}, C–O stretching 1076.93, 1138.53, 1204.08 cm^{-1} (alcoholic group), C=O – 1707.57 cm^{-1} (ketone group), C–H – 2933.43 cm^{-1} and C=C – 1564.18 cm^{-1} and thus confirmed the drug-excipient compatibility. These FTIR bands of the drug remain intact in both the spectra of the drug and physical mixture, illustrating absence of interaction between drug and polymers used

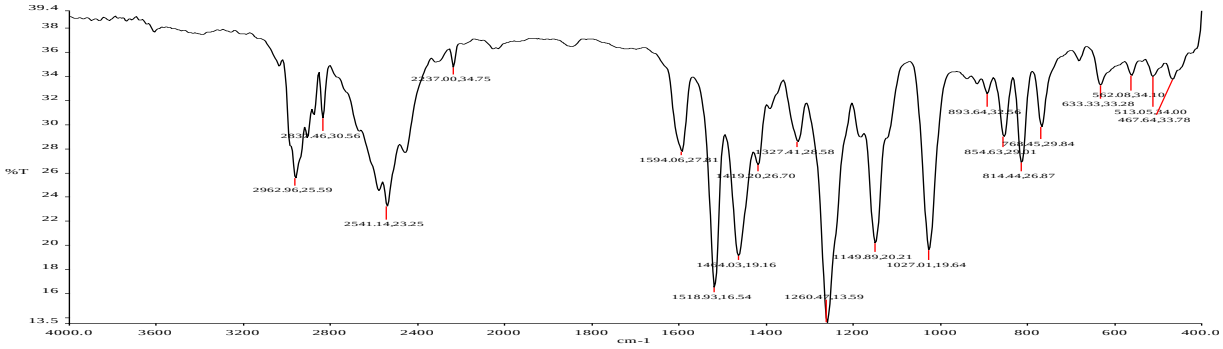

Figure 3: FTIR Spectrum of sumatriptan

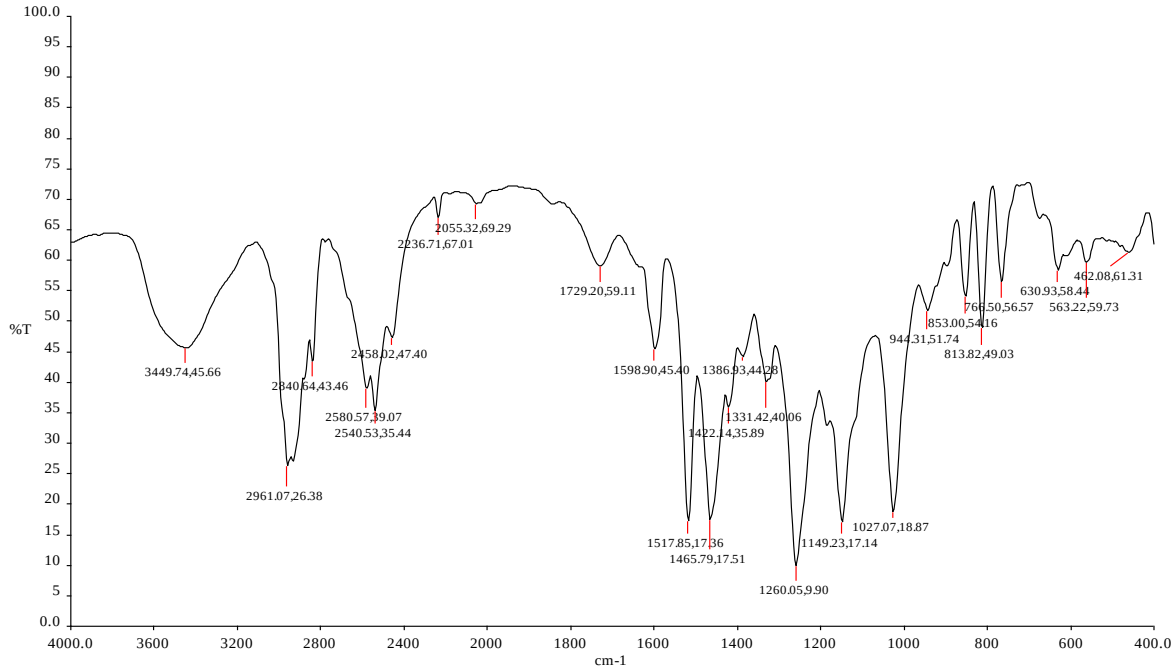

Figure 4: FTIR Spectrum of physical mixture of drug with Carbopol 940P

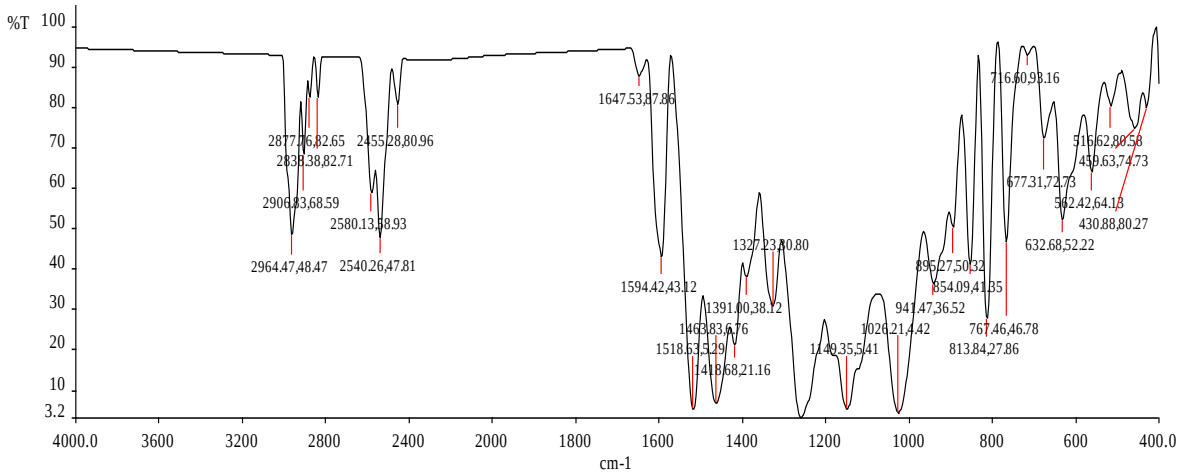

Figure 5: FTIR Spectrum of physical mixture of drug with liquid paraffin

Characterization of emulgel:

Physical appearance:

The formulated emulgels were examined for their color, homogeneity, consistency and phase separation after 24 hr of preparation. They were white, homogenous, transparent to white opaque with a smooth homogeneous appearance and there was no significant phase separation observed in the formulations.

Measurement of pH:

Emulgel formulations was in the range of 6.09 to 6.43, which lies in the normal pH range of the skin and would not produce any skin irritation. The results are represented in table-3.

Spreadability:

One of the essential criteria for an emulgel is that it should possess good spreadability. Spreadability is an important factor in therapy and it is shown as index of ease of application. The delivery of the correct dose of the drug depends highly on the spreadability of the formulation. The spreadability of sumatriptan emulgel formulations was found to be in range of 95 g.cm/min to 126 g.cm/min for the F1- F8 formulations and the results are given in the table-3.

Drug Content Determination:

Drug content of the formulations were determined by using standard plot and the values were given in the

table-3 and the values ranged from 94.54% to 97.75%.

Viscosity:

The viscosity of all the formulations was found between 340 cps to 792 cps. As the concentration of gelling polymer increases, the viscosities of formulations were also increases. The results were shown in the table 3.

Table 3: Evaluation parameters of prepared emulgels

S. NO	Formulation code	pH	Spreadability (g.cm/min)	Drug content%	Viscosity (cps)
1	F_1	6.09	95	94.54	340
2	F_2	6.33	110	97.23	389
3	F_3	6.17	104	96.45	469
4	F_4	6.40	126	94.33	538
5	F_5	6.28	113	97.75	596
6	F_6	6.45	117	96.52	637
7	F_7	6.30	120	95.47	664
8	F_8	6.15	115	94.21	792

Extrudability:

Among the gel formulations F1 to F6, more than 90% of the contents were extrudable indicating they have excellent extrudability except F7 and F8 as 80% of the contents were extrudable and indicated that they have good extrudability. (>90% extrudability: excellent, >80% extrudability: good, >70% extrudability: fair).

Centrifugation:

The prepared emulgels were subjected to centrifugation test to determine the physical stability and there was no phase separation or creaming observed during this test which indicated that the formulations were stable.

***In-vitro* drug release study:**

The study showed the release of the drugs from its emulsified gel formulations. The drug release of the selected batches were shown in the Figure 6. The better release of the drug from all emulgel formulation can be observed and the emulgel formulation can be ranked in the order of F4> F5> F3> F1> F6> F7> F8. Among the formulations, F4 showed better release (97.87%) characteristics than other formulations. Of the developed formulations F4 has shown the uniform and good drug release of 97.87% at the end of 4 hrs.

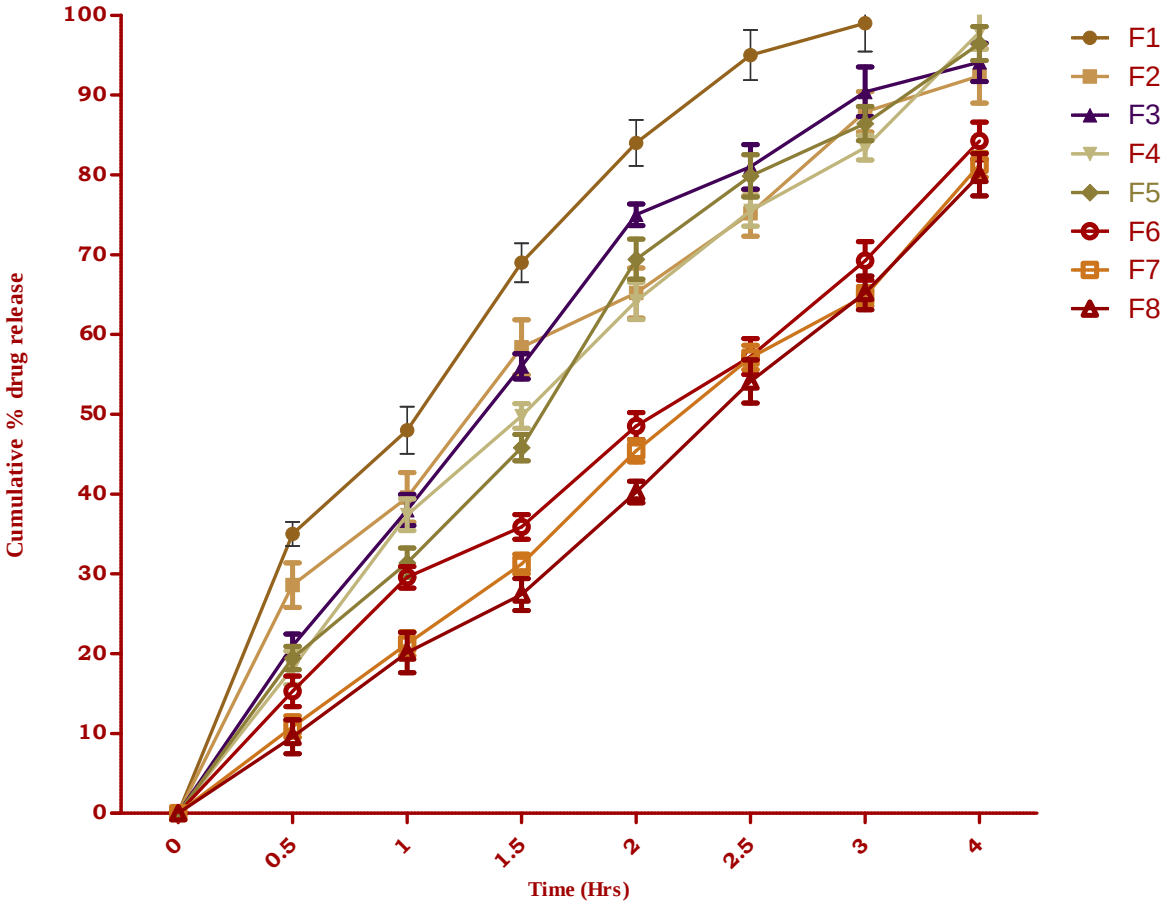

Figure 6: *In vitro* cumulative % of drug release of emulgel formulations F1to F8

Drug release Kinetics:

From the kinetic data, the formulationsF2, F3, F8 shows drug release by korsmeyer-Peppas model. The regression values for these formulations range from 0.9871-0.9962. The formulation F1, F5, F6, F7shows drug release by Higuchi i.e., drug release is by diffusion process. The optimized formula F4shows drug release by zero order kinetics (R^2 =0.951) and higuchi mechanism i.e., diffusion (R^2 =0.968). The 'n' values of korsmeyer Peppas model are in the range of 0.896 to 1.41. It indicates that drug release is by erosion of polymeric chain.

Table 4: Kinetic parameters for the *in-vitro* release of sumatriptan from different emulgel formulations

Formulation	Zero-order	First-order	Higuchi	Korsmeyer-Peppas
	R^2			N
F1	0.907	0.963	0.941	0.896
F2	0.927	0.978	0.939	0.993
F3	0.943	0.957	0.928	0.981
F4	0.951	0.948	0.968	1.191
F5	0.943	0.951	0.977	1.41
F6	0.904	0.942	0.966	0.876
F7	0.896	0.924	0.959	0.934
F8	0.921	0.943	0.931	1.315

***Ex-vivo* release studies:**

The study was carried out only on optimized formulation F4 and showed the drug release from its emulsified gel was found to be 52.4 % respectively in 4 hr.

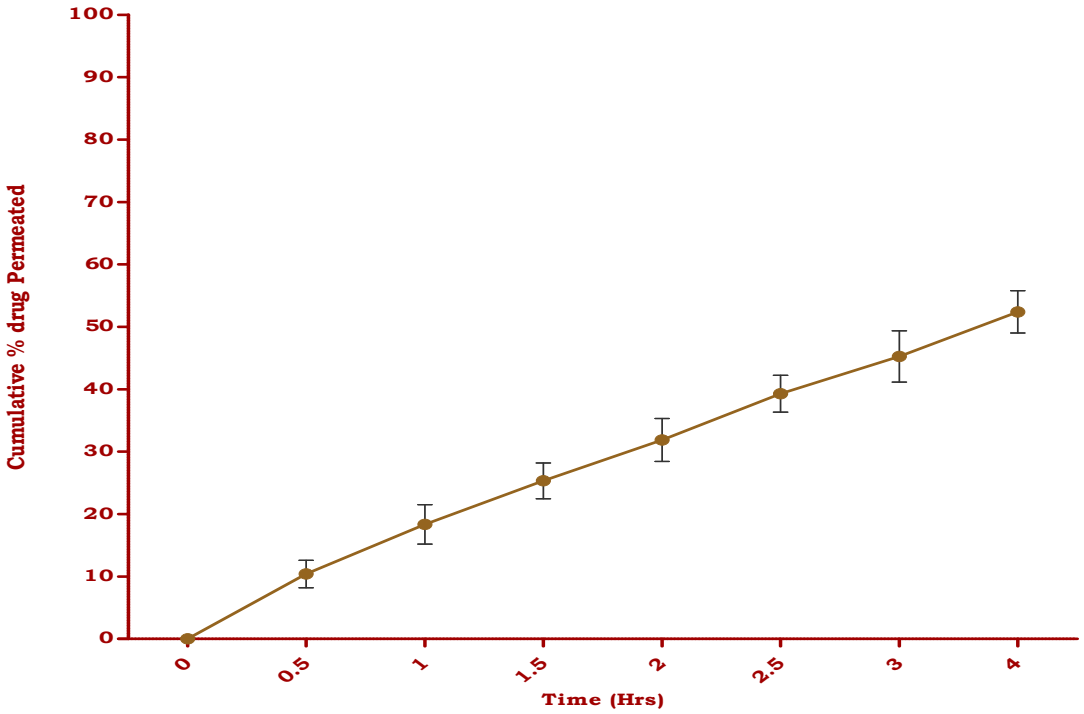

Figure 7: *Ex vivo* cumulative % of drug permeation studies of most satisfactory formulation F4

***In vitro ex vivo* correlation between cumulative % drug released *in vitro* and % drug permeated *ex vivo* of optimized formulation of emulgel**

Cumulative percentage of drug released *ex vivo* through the rat skin was correlated against cumulative percentage of drug released using *in vitro* release tests for optimized formulation F4. Figure 8 shows the relationship between the percentage of drug released *ex vivo* and percentage of drug released *in vitro*. The straight line and the high correlation coefficient of 0.9935 proved the good correlation between *in vitro* drug release and *ex vivo* drug release studies. Hence by considering the complete difference in the test conditions of *in vitro* and *ex vivo* release studies, the high correlation and coincidence of *in vitro* and *ex vivo* release profiles, it can be concluded that emulgels could be a useful carrier in improving the bio availability.

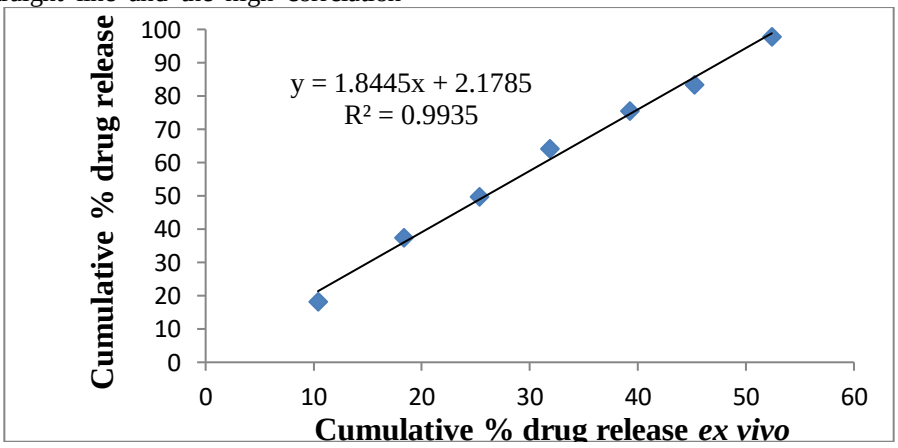

Figure 8: Correlation *between In-vitro* and *ex-vivo* drug release of the optimized formulation

Stability study:

All the prepared emulgel formulations were found to be stable upon storage for 2 month, no change was observed in their physical appearance, pH, rheological properties and drug content.

CONCLUSION:

The present study was carried out with the aim to prepare an emulgel formulation for topical delivery of sumatriptan. Emulgel of sumatriptan were developed by using aqueous, oil phases, gelling agent such as Carbopol 940P using modified conventional method. Developed emulgel formulations possessed the required physicochemical properties such as good physical appearance, drug content uniformity, excellent spreadability and extrudability.

All the formulations F1-F8 have passed all the evaluations with good values. The formulations were found to be stable and homogenous in nature, pH of the formulations suggest that values were within the limits of the skin pH. *In-vitro* releases of the tests formulations were performed to determine drug release rate from emulgel. F4 were subjected to stability studies which showed satisfactory results. Stability study of the formulation showed no significant changes in the drug content as well as physical characteristics. The formulation (F4) has fulfilled the objectives of the present study like increasing the bioavailability, reduction in the frequency of administration, improved patient compliance.

Considering the various dermatological topical preparation with various advantages and disadvantages, emulgels serve as the better alternative of the present available marketed topical formulation for delivery of hydrophobic drugs.

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