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Formulation and Evaluation of Self Emulsifying Emulsion of Ketaconazole

Shashank Khugshal*[1], Ashutosh Badola[1], Preeti Kothiyal[2], Shweta Baluni[3]
1. Division of Pharmaceutical Sciences, Shri Guru Ram Rai institute of Technology, Uttarakhand technical university, Dehradun (Uttarakhand), India.

ABSTRACT

The aim of present work was to develop a self emulsifying emulsion of ketaconazole for the topical delivery system which is useful in the treatment of fungal infection. Prepared SEDDS was investigated for different parameters. All the prepared SEDDS showed acceptable physical properties concerning colour, viscosity, melting point etc. The results of *in -vitro* drug release showed that carbopol 934 was the formula of choice as it showed better drug release & antifungal activity. The percentage cumulative drug released was determined by UV spectrophotometer. FTIR studies revealed that drug and all excipients are compatible. The data obtained from *in- vitro* permeation studies was treated by various conventional mathematical models (zero order, first order, Higuchi and Korsmeyer- peppa's) to determine the release mechanism from the designed self emulsifying formulations. Selection of a suitable release model was based on the values of R^2 (correlation coefficient), k (release constant) obtained from the curve fitting of release data. It was found that all the formulations follows the first order kinetics. The regression coefficients for the all formulations F1 to F4 of Higuchi plot was found to be almost linear.

Key words: SEDDS, ketaconazole, antifungal drug, topical drug delivery.

*Corresponding Author Email: shankykhugshal001@gmail.com
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INTRODUCTION

Self emulsifying drug delivery system (SEDDS)

Self emulsifying drug delivery system (SEDDS) are defined as the of mixtures isotropic of synthetic oils or natural, liquid or solid surfactants, or alternatively, one or more hydrophilic solvents and co-solvents/surfactants that had unique ability of forming fine oil-in-water (o/w) micro emulsions upon mild agitation which is followed by dilution in aqueous media, such as GI fluids[1]. SEDDS formulations could be simple binary systems: lipophilic phase, surfactant and drug, or lipophilic phase and drug. The SEDDS formation requires use of co-surfactant in a order to generate a micro emulsion. Formulations of SEDDS are characterized by in vitro lipid droplet sizes of 200 nm^{-5} mm and the dispersion having a turbid appearance. Drugs in a large number has being discovered today are highly lipophilic and poorly soluble in water. Bioavailability showen by them are erratic and poor[2]. Self-emulsifying drug delivery systems (SEDDS) are the mixtures of surfactants and oils, ideally isotropic, and sometimes containing co-solvents, which thereby emulsify spontaneously to produce fine oil-in-water emulsions under gentle agitation[3] which are when introduced into aqueous phase. SMEDDS formulation is in theory, comparatively simple. The main step is to find a suitable oil surfactant mixture which can dissolve the drug within the required therapeutic concentration. The mixture of SMEDDS can be filled in either hard or soft gelatin capsules. A typical formulation of SMEDDS contains oils, surfactants and if required an antioxidants. Often co-surfactants and co-solvents are added to improve the formulation characteristics. In the present topic, focus will be on lipid based drug delivery systems (e.g. Self-Emulsifying Drug Delivery systems (SEDDS)). Emulsion particles can be of either nano-size or micro-size, depending on the system composition. These formulations circumvent the dissolution step in the gastro-intestinal tract, but are still dependent on digestion.

1.2.1 Advantages: [4,5]

- Oral bioavailability is enhanced
- Reduction in the dose.
- Drugs Protection from hostile environment in the gut.
- Targeting of drugs
- Controlled drug delivery
- Variability Reduced including food effects.
- Possibility in achieving the Reproducibility.
- Patient compliance.

1.2.2 Disadvantages: [6,7]

- There is no accurate predictive in vitro models for assessment of the formulations.
- Porttability and stability is low.
- In the formulations large quantity of surfactants can induce GI irritation.

MATERIALS AND METHODS :

Ketoconazole was obtained as a gift sample from Windlas medicare Pvt. Ltd. Dehradun, India. Carbapole 940, carbapole 934, Span 20, Tween 20, Ethanol, Poly oxylglycerides was purchased from Central drug house Pvt. Ltd. Delhi (IND).

Preformulation studies:

Preformulation testing is the first step in the rationale development of dosage form to a drug. It can be defined as the investigation of physical and chemical properties if drug substance alone or in combination with excipients. The overall objectives of preformulation studies is to generate information useful in formulation of developing stable and bioavailable dosage form which can be mass produced.

Identification tests

Identification of drug through Fourier transform infrared (F.T.I.R.):-

Infrared spectrum of ketaconazole was determined by using Fourier Transform Infrared Spectrophotometer using KBr disks method. The sample (0.5 to 1.0 mg) is finely grounded and intimately mixed with approximately 100 mg of dry potassium bromide powder. Grinding and mixing can be done with mortar and pestle. The mixture is then pressed into a transparent disk in an evacuable die at sufficiently high pressure. Suitable KBr disks or pellets can often be made using a simpler device such as a hydraulic press. The base line correction was done using dried potassium bromide. Then, the spectrum of dried mixture of drug and potassium bromide was scanned from 2000 cm^{-1} to 400 cm^{-1} compare with reference graph. FTIR has been used to assess the interaction between drug and polymers.

Organoleptic properties:

Organoleptic properties of ketaconazole were characterization by descriptive terminology, the color, odour and taste of the drug were recorded.

Determination of Melting Point: The sample was loaded in to sealed capillary (melting point capillary) which was then placed in melting point apparatus. The sample was then heated and as the temperature increase the sample was observed to detect the phase change from solid to liquid phase. The temperature at which the phase changes occur gives the melting point.

Determination of solubility:

The solubility of the drug were checked in different solvents like distilled water, buffers and organic solvents and recorded. This might be helpful in selection of a suitable solvent to dissolve drug as well as excipients used in formulations. A definite quantity (10mg) of the drug was dissolved in 10ml of each investigated solvent at room temperature

Preparation of calibration curve of ketaconzole

A stock solution of 10µg of ketaconazole was prepared in methanol and scanned by UV spectrophotometer (200-400nm) for the determination of λ max of ketaconazole. For selection of media the criteria employed were sensitivity, ease of sample preparations, solubility of drug and cost of solvents and applicability of method to various purposes. An UV spectroscopic scanning run (200-400nm) was carried out to select the best UV wavelength for detection of ketaconazole in methanol. The analysis was carried out using Distilled water as blank. Absorbance of ketaconazole was determined.

Calibration Curve of ketaconazole :

Accurately weight 50 mg of drug was dissolved in 50 ml of methanol and thus 1000 mcg solution was prepared now from this different dilutions were made and different concentrations were prepared in the range of 1-25 mcg/ml of ketaconazole in methanol for standard curve.

Partition coefficient:

The partition coefficient of ketaconazole was determined in CCL4: HCL buffer (0.1) briefly an excess amount of ketaconazole was added in to 50ml each of carbon tetra chloride aqueous phase. The mixture was shaken for 24 hrs until equilibrium was reached. Phases were separated in a separating funnel and the aqueous phase was filtered through 0.2µ filter, suitably diluted and amount of ketaconazole solubilized in aqueous phase was determined by measuring absorbance at 278nm using UV spectrophotometer.

The partition coefficient of ketaconazole was calculated from the ratio between the concentration of ketaconazole in organic and aqueous phase using following:-

$$\mathbf{P\ o/w = (C_{oil}/C_{aqueous})\ equilibrium}$$

Drug - excipient Compatibility Study:

The objective of this investigation was to identify a stable storage condition for drug in solid state and identification of compatible excipients for its information. This can be confirmed by carrying out by infrared light absorption scanning spectroscopy studies (IR). Drug and polymer was mixed in the equal ratio and finally grounded and intimately mixed with approximately 100

mg of dry potassium bromide powder. Grinding and mixing can be done with mortar and pestle. The mixture is then pressed into a transparent disk in an evacuable die at sufficiently high pressure. Suitable KBr disks or pellets can often be made using a simpler device such as a hydraulic press. The base line correction was done using dried KBr. Then, the spectrum of dried mixture of drug and potassium bromide was scanned from 2000cm^{-1} to 400 cm $^{-1}$.

Evaluation parameters for the formulation

Physical appearance:

The prepared emulsion preparations were examined visually for their color, homogeneity, consistency.

Dispersibility test

The efficiency of self-emulsification of oral nano or micro emulsion is assessed using a standard USP XXII dissolution apparatus 2. One milliliter of each formulation was added to 500 mL of water at 37 ± 0.5 ^{0}C. A standard stainless steel dissolution paddle rotating at 50 rpm provided gentle agitation. The in vitro performance of the formulations is visually assessed using the following grading system:

Grade A: Rapidly forming (within 1 min) nano emulsion, having a clear or bluish appearance.

Grade B: Rapidly forming, slightly less clear emulsion, having a bluish white appearance.

Grade C: Fine milky emulsion that formed within 2 min.

Grade D: Dull, grayish white emulsion having slightly oily appearance that is slow to emulsify (longer than 2 min).

Grade E: Formulation, exhibiting either poor or minimal emulsification with large oil globules present on the surface. Grade A and Grade B formulation will remain as nano emulsion when dispersed in GIT. While formulation falling in Grade C could be recommend for SEDDS formulation.

Viscosity Determination

The SEDDS system is generally administered in soft gelatin or hard gelatin capsules. So, it can be easily pourable into capsules and such system should not too thick to create a problem. The rheological properties of the micro emulsion are evaluated by Brookfield viscometer. This viscosities determination confirm whether the system is w/o or o/w. If system has low viscosity then it is o/w type of the system and if a high viscosity then it is w/o type of the system.

Refractive Index and Percent Transmittance

Refractive index and percent transmittance proved the transparency of formulation. The refractive

index of the system is measured by refractometer by placing drop of solution on slide and it compare with water (1.333). The percent transmittance of the system is measured at particular wavelength using UV spectrophotometer keeping distilled water as blank. If refractive index of system is similar to the refractive index of water (1.333) and formulation have percent transmittance> 99 percent, then formulation have transparent nature.

Techniques for Solid Formulations

Techniques are chosen on the basis of properties of lipid excipients. The techniques reviewed here under facilitate the transformation of liquid or semi-solid formulations into solid particles (powders, granules or pellets) which could subsequently be filled into capsules, sachets or compressed into tablets.

Spray Cooling

The molten droplets are sprayed into cooling chamber, which will congeal and re-crystallize into spherical solid particles that fall to the bottom of the chamber and subsequently collected as fine powder. The fine powder may then be used for development of solid dosage forms tablets or direct filling into hard shell capsules. Many types of equipment are available to atomize the liquid mixture and to generate droplets: rotary, pressure, two-fluid or ultrasonic atomizers.

Spray Drying

Spray drying is defined as a process by which a liquid solution is sprayed into a hot air chamber to evaporate the volatile fraction. Polyoxylglycerides (lauroyl or stearoyl) have been used alone or in combination with a solid carrier (silicon dioxide) to form microparticles of etoricoxib and glibenclamide. Dry emulsion technology solves the stability problems associated with classic emulsions (phase separation, contamination by microorganism, etc.) during storage and helps also avoid using harmful or toxic organic solvents. Dry emulsions may be redispersed into water before use. Medium chain triglycerides are commonly used as oil phase for these emulsions.

Melt Extrusion/ Spheronisaton

Extrusion is a process of converting a raw material with plastic properties into a product of uniform shape and density by forcing it through a die under controlled temperature, product flow and pressure conditions. This approach has been successfully tried for 17β- estradiol and two model drugs with surfactants such as sucrose monopalmitate, lauroyl polyoxylglycerides and polysorbate80 (Tween® 80). Gelucire 44/14 to be used directly in the core of the formulation matrix. An innovative “systemin cylinder” molding technique was recently employed to develop a dual purpose (enhanced bioavailability and controlled release) formulation with propranolol

hydrochloride. Melt extrusion is a solvent free process that allows high drug loading as well as content uniformity for low dose high potency actives.

Supercritical Fluid Based Method

Lipids may be used in supercritical fluid based methods either for coating of drug particles, or for producing solid dispersions. For environmental reasons, the preferred supercritical fluid of choice is supercritical carbon dioxide. Examples include controlled release applications using glyceryltrimyristate (Dynasan™ 114) and stearoylpolyoxyl glycerides (Gelucire®50/02).

Solid Lipid Nanoparticles and Nanostructure Lipid Carriers

SLN and NLC are two types of submicron size particles (50– 1000 nm) composed of Physiologically tolerated lipid components. SLN are produced by high-pressure homogenization of the solid matrix and drug with an aqueous solution of the glyceryldibehenate as solid lipid matrix and poloxamers 188 or polysorbates 80 as surfactants. They typically contain liquid lipid excipients such as medium chain triglycerides in addition to classic components of SLN. They have been mainly used for controlled-release applications in oral 86, intravenous 87 or topical route.

***In-Vitro* Release/Permeation Studies**:

Using Franz diffusion cell *In-vitro* release studies were carried out.

Drug release kinetic study

The mechanism of drug release from the topical gel is analyzed by fitting the release data to following equations

Zero – order equation:

$Q = k_0 t$

Where, Q is the amount of drug released at time t

k_0 is the zero – order release rate.

First – order equation:

$\text{In } (100 - Q) = \text{In } 100 - k_1 t$

Where, Q is the percent of drug release at time t

k_1 is the first – order release rate constant.

Higuchi's equation:

$Q = k_2 \sqrt{t}$

Where, Q is the percent of drug release at time t

k_2 is the diffusion rate constant.

Pharmaceutical applications of Multiple Emulsions:

a. They can mask the bitter taste and order of drug e.g. chlorpromazine
b. Multiple emulsions are used in food .
c. They can be used to prolong the release of drug thus providing sustained release action.
d. Essential nutrients like carbohydrates, fats and vitamins can all be emulsified and can be administered to bed ridden patient as sterile intravenous injection.
e. Emulsion provides protection to drugs which are susceptible to oxidation or hydrolysis.
f. Intravenous emulsions of contrast media have been developing to assist in diagnosis.
g. Increase in dosing interval.
h. Hydrophilic as well as hydrophobic drug can be entrapped.

RESULTS AND DISCUSSIONS

Four formulation of ketaconazole were formulated using different drug polymer ratio. The formulation is subjected to evaluation parameter like viscosity, solubility, melting point, in vitro drug release study etc.

Preformulation studies:

Organoleptic properties of drug:

Table 1: Results of Organoleptic properties

S.no.	Properties	Result
1	Description	Solid
2	Color	White, off white crystalline powder
3	Taste	Tasteless
4	Odour	Odourless

Solubility of drug:

Table No. 2: Solubility of ketaconazole formulation

S.NO.	Solvent	Solubility	Parts of solvent required for one part of solute (ppm)
1	Water	Insoluble	0.0866
2	Ethanol	Soluble	0.088
3	Dimethyle sulfoxide	Soluble	0.3092

Melting point: The melting point of ketaconazole was found to be 150-154ºC. This value is same as that of the literature citation of 148-152ºC.

Table no.3: Results of Melting point determination

S. No.	Method used	Experimental value	Literature value
1.	Capillary method	150-154ºC	148-152ºC

Partition Coefficient: It is a dibasic compound [pka(1)= 6.51, pka(2)=2.94]

Calibration curve of ketaconazole:

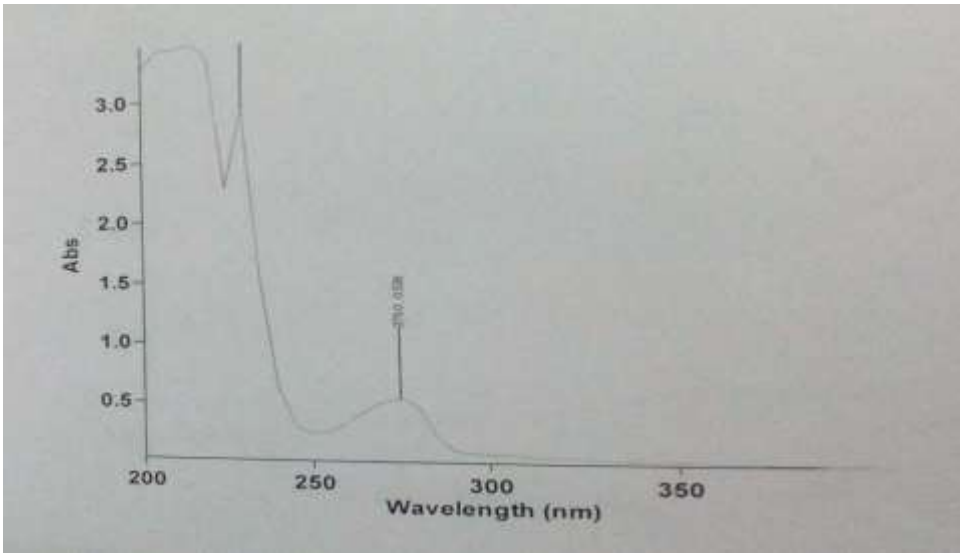


Fig no.1 UV Spectrum of ketaconazole

Table No.4: Data for calibration curve of ketaconazole:

S. No.	Concentration (µg/ml)	Absorbance
1	0	0
2	0.1	0.0208
3	0.2	0.0470
4	0.4	0.1400
5	0.6	0.1983
6	0.8	0.2622
7	1.0	0.3423

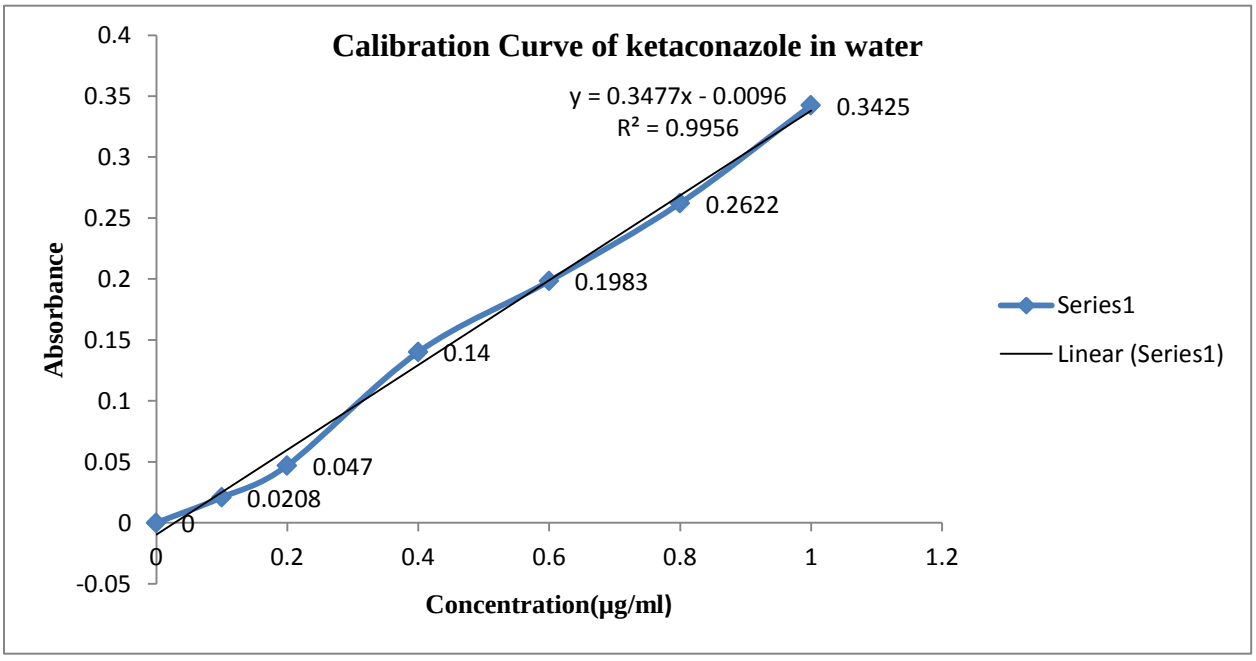


Fig. no.2: Calibration curve of ketaconazole

Standard stock solution of ketaconazole was prepared by dissolving accurately weigh 50 mg of ketaconazole in 50 ml of 0.1 N HCL solution.

Determination of λ max of ketaconazole

From the standard stock 10µg/ml was scanned under spectrum mode for 200- 400 nm wavelength range and a sharp peak was obtained at 275 nm.

Identification of drug:

Identification of sample ketaconazole through FTIR

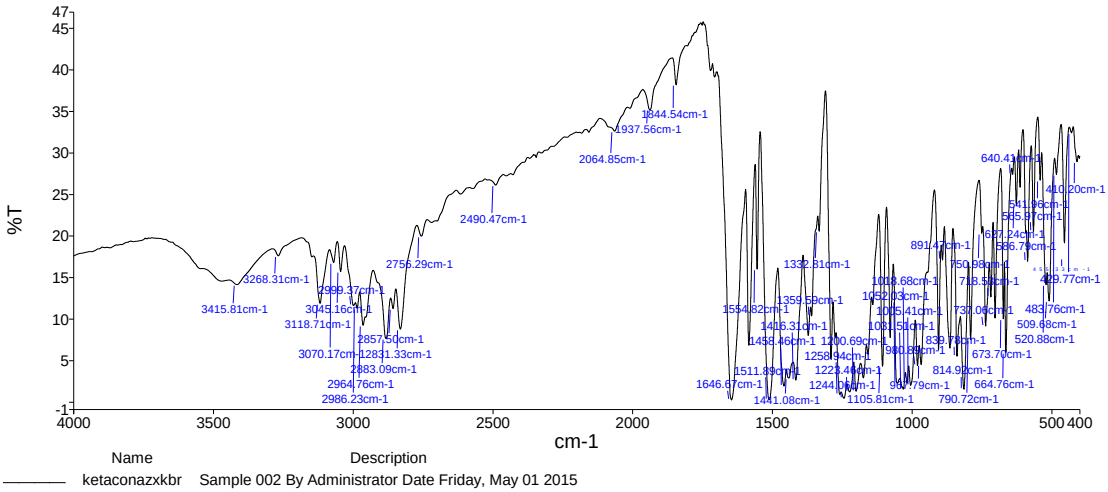


Fig no.3: FTIR of sample ketaconazole

FTIR of standard ketaconazole

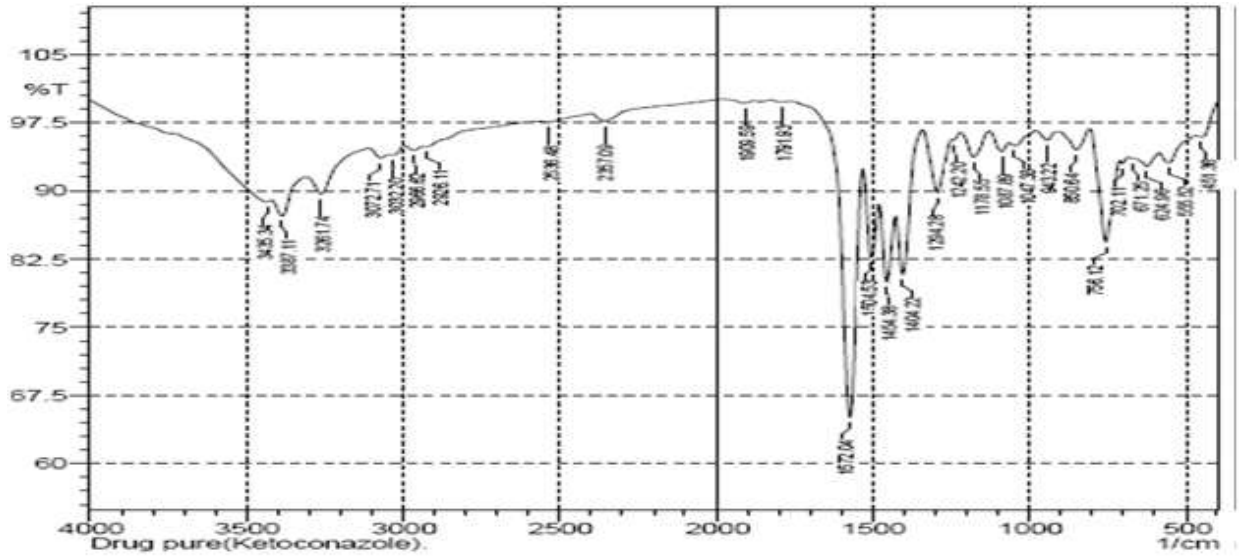


Fig no. 4. : FTIR Spectrum of standard ketaconazole

Table no..5: Characteristics peaks of ketaconazole

S. No.	Wavenumber cm^{-1}	Functional Group	Stretching/Bending
1	2857	C-H	Stretching
2	1458	C-H	Deformation
3	737	C-C	Deformation

Spectral Studies

Compatibility study of drug with polymers:

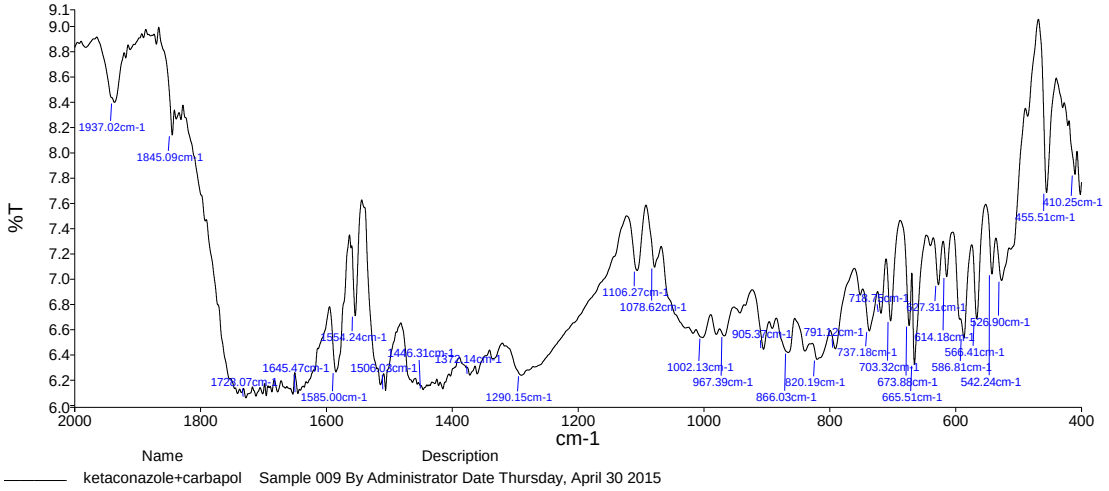


Fig 5: F.T.I.R. spectra of ketaconazole+carbopol 934

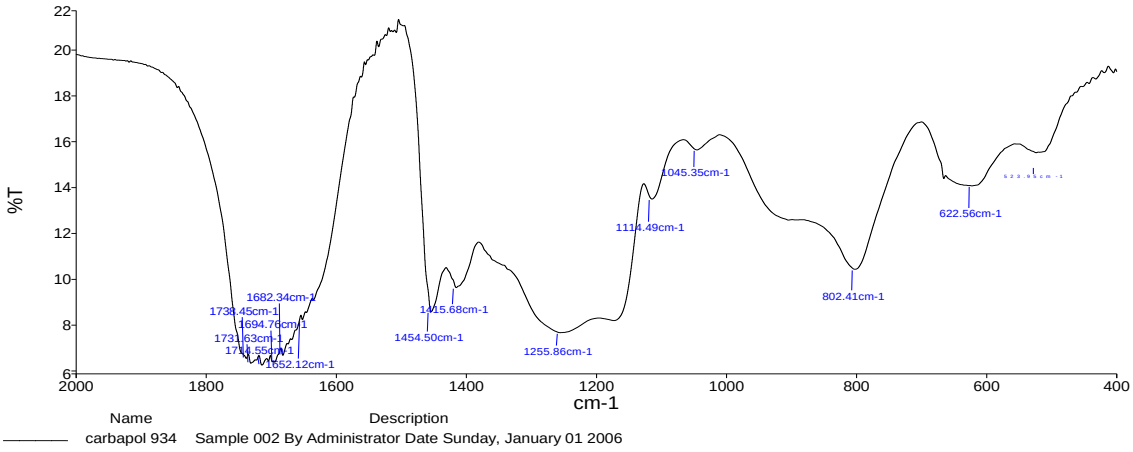


Fig no.6: FTIR spectra of carbapol 934

Table No. .6: FTIR interepretation of Carbapole 934

S. No.	Wavenumber cm^{-1}	Functional Group	Stretching/Bending
1.	802	C-H	Deformation
2.	1415	C-H	Deformation
3.	1652	C=O	Stretching

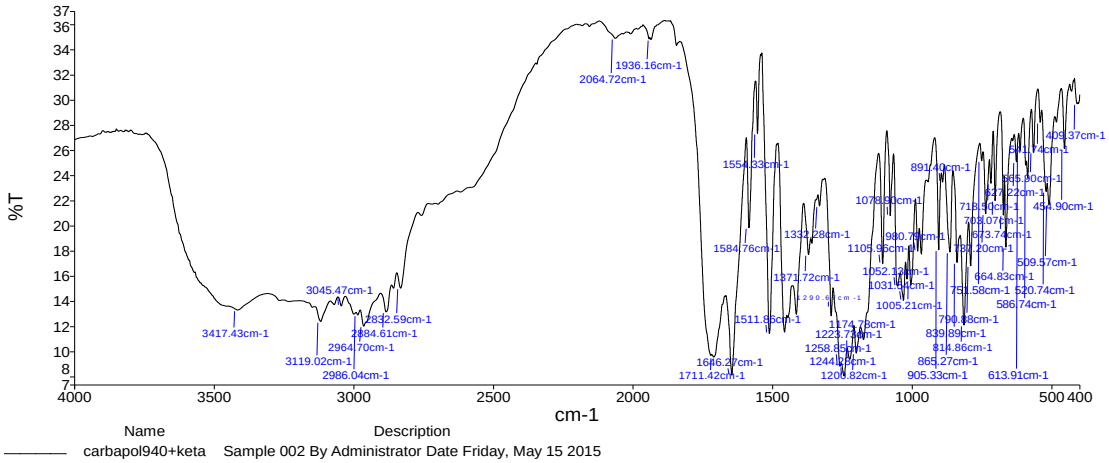


Fig no.7: F.T.I.R. Spectra of ketaconazole+ carbopol 940

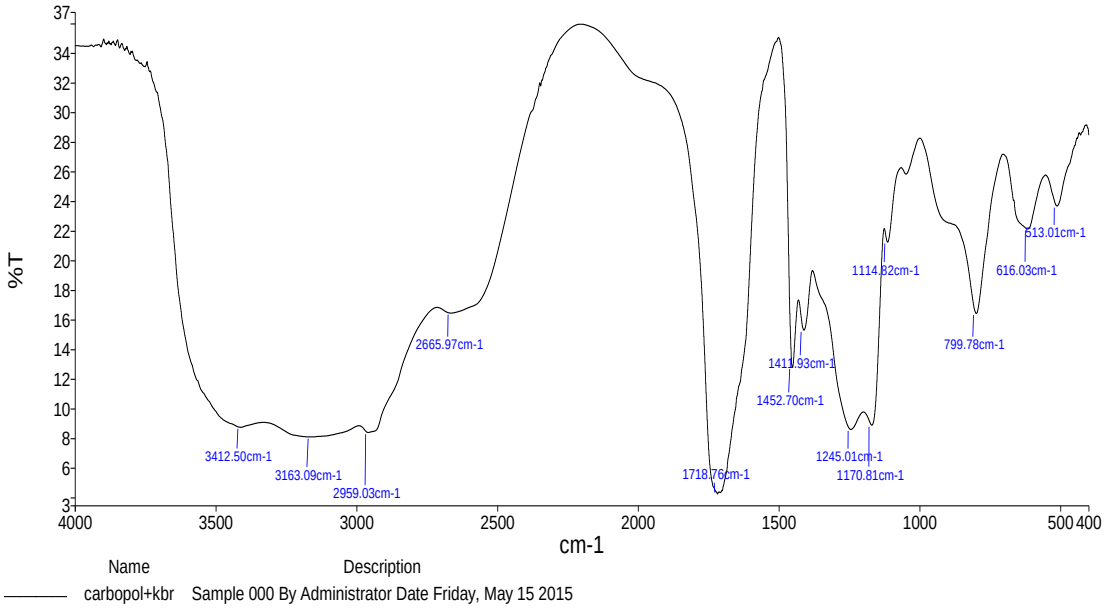


Fig. no.8: FTIR spectra of carbapol 940

Table No. 7: FTIR interpretation of Carbapole 940

S. No.	Wavenumber cm^{-1}	Functional Group	Stretching/Bending
1.	3412	N-H	Stretching
2.	1718	C=O	Stretching
3.	1245	C-O	Stretching

The drug-polymer interactions shows that there was no major shifts in the absorption bands(peaks) of in presence of polymer and it was observed that all the characteristics peaks of drug is present in the combination of drug and polymer spectra indicating the compatibility of drug with the polymer used.

Composition of ketaconazole

Table No. 8: Composition of ketaconazole formulation(%w/w)

S.No.	Contents	F1	F2	F3	F4
1	Ketaconazole	1	1	1	1
2	Carbopol 940	-	-	1	1
3	Carbopol 934	1	1	-	-
4	Polyoxyleglycertes	0.45	0.45	0.45	0.45
5	Span 20	1	1	1	1
6	Tween 20	0.5	0.5	0.5	0.5
7	Light liquid paraffin	7.5	7.5	7.5	7.5
8	Methyl paraben	0.03	0.03	0.03	0.03
9	Propyl paraben	0.01	0.01	0.01	0.01
10	Water	q.s	q.s	q.s	q.s

Viscosity: From the above table the viscosity of ketaconazole formulation is in between 23.24 to 29.65. Viscosity has great significance with respect to the performance of topical products.

Table No. 9: Viscosity of ketoconazole formulation

Formulation	Viscosity
F1	23.24±0.91
F2	25±0.5
F3	27.65±1.18
F4	29.65±1.52

Refractive index & Percentage transmission: From the above table the refractive index of ketaconazole formulation is in between 1.331 to 1.335 and percentage transmission is in between 99.6 to 100.9.

Table No. 10: Refractive index & %transmission

Formulation	Refractive index	Percentage transmission
F1	1.334	100.9
F2	1.334	99.6
F3	1.331	100.6
F4	1.335	99.8

***IN-VITRO* RELEASE STUDY**

The release of ketaconazole formulation worried according to change in polymers. The release of drugs from formulation can be ranked in following order, F2 > F1 >F4>F3 where the amount of drug release after 8 hours were 67.18%, 62.34%, 53.68%, 52.52% respectively. It has been concluded that the formulation with carbapol 934 shows maximum release. The cumulative %

drug release profile of all the formulation batches has been shown in table no. and graph is plotted in between cumulative % drug release v/s time.

Table No. 11: *In-vitro* drug release study of ketaconazole formulation

S.No.	Time(hrs)	Cumulative % drug release			
		F1	F2	F3	F4
1.	0	0	0	0	0
2.	1	6.07	4.86	8.513	6.71
3.	2	13.67	12.22	19.536	9.83
4.	3	26.82	19.52	24.425	15.67
5.	4	34.19	24.42	24.105	23.14
6.	5	42.75	32.97	28.105	28.79
7.	6	51.312	41.56	32.99	31.48
8.	7	57.43	53.73	41.565	50.69
9.	8	62.34	67.18	52.52	53.68

Table no.12 : *In- vitro* permeation profile of ketaconazole from Formulation F1

S.No.	Time (hrs)	$\sqrt{T}$	Log T	% Cumulative drug release	% Cumulative drug remain	Log % Cumulative drug remain	Log % Cumulative drug release
1.	0	0	-	0	100	2	-
2.	1	1	0	6.07	93.93	1.972	0.783
3.	2	1.414	0.3	13.67	86.33	1.936	1.135
4.	3	1.732	0.47	26.82	73.18	1.864	1.428
5.	4	2	0.6	34.19	65.81	1.818	1.533
6.	5	2.236	0.69	42.75	57.85	1.762	1.630
7.	6	2.449	0.77	51.312	48.688	1.687	1.710
8.	7	2.645	0.84	57.43	42.57	1.629	1.759
9.	8	2.828	0.9	62.34	32.66	1.575	1.794

Table no.13: *In- vitro* permeation profile of ketaconazole from Formulation F2

S.No.	Time (hrs)	$\sqrt{T}$	Log T	% Cumulative drug release	% Cumulative drug remain	Log % Cumulative drug remain	Log % Cumulative drug release
1.	0	0	-	0	100	2	-
2.	1	1	0	4.86	95.14	1.978	0.686
3.	2	1.414	0.3	12.22	87.78	1.943	1.087
4.	3	1.732	0.47	19.52	80.48	1.905	1.290
5.	4	2	0.6	24.42	75.58	1.878	1.387
6.	5	2.236	0.69	32.97	67.03	1.826	1.518
7.	6	2.449	0.77	41.56	58.44	1.766	1.618
8.	7	2.645	0.84	53.73	46.27	1.665	1.730
9.	8	2.828	0.9	67.18	32.82	1.516	1.827

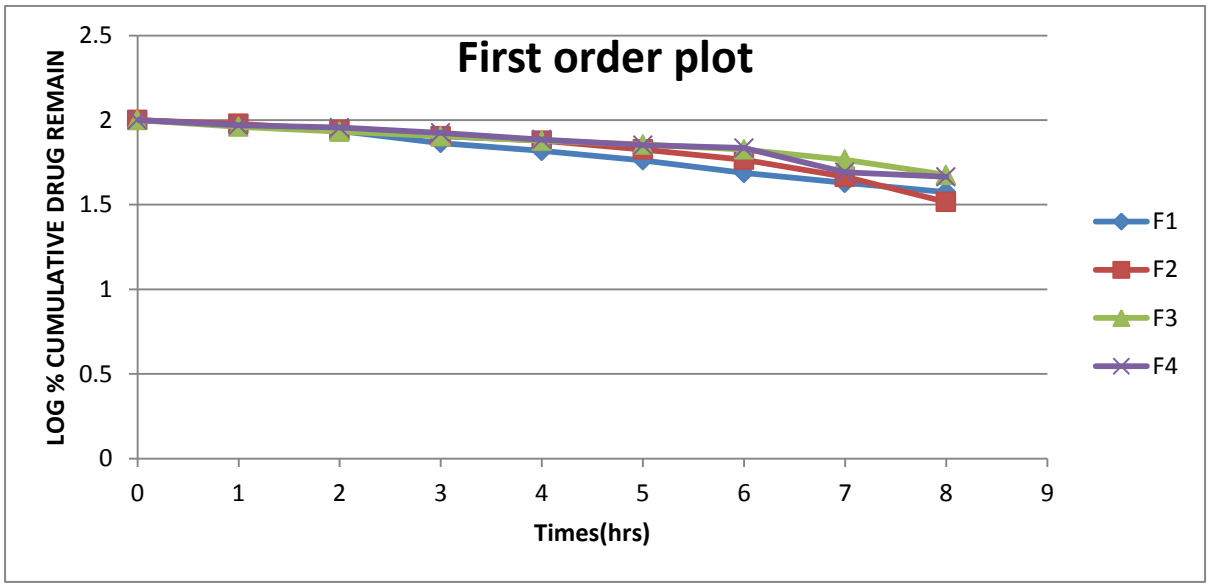
Table no. 14 : *In- vitro* permeation profile of ketaconazole from Formulation F3

S.No.	Time (hrs)	$\sqrt{T}$	Log T	% Cumulative drug release	% Cumulative drug remain	Log % Cumulative drug remain	Log % Cumulative drug release
1.	0	0	-	0	100	2	-
2.	1	1	0	8.513	91.487	1.961	0.930
3.	2	1.414	0.3	14.639	85.361	1.931	1.165
4.	3	1.732	0.47	19.536	80.464	1.905	1.290
5.	4	2	0.6	24.425	75.575	1.878	1.387
6.	5	2.236	0.69	28.105	71.895	1.856	1.448
7.	6	2.449	0.77	32.99	67.01	1.826	1.518
8.	7	2.645	0.84	41.565	58.435	1.766	1.618
9.	8	2.828	0.9	52.52	47.48	1.676	1.720

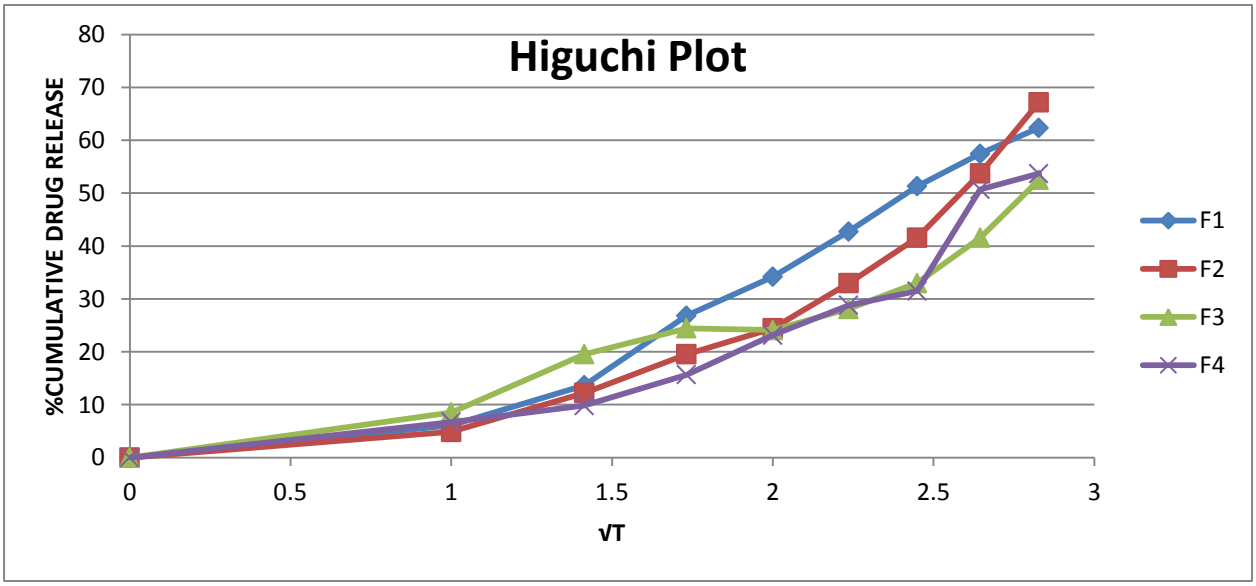
Table no.15 : *In- vitro* permeation profile of ketaconazole from Formulation F4

S.No.	Time (hrs)	$\sqrt{T}$	Log T	% Cumulative drug release	% Cumulative drug remain	Log % Cumulative drug remain	Log % Cumulative drug release
1.	0	0	-	0	100	2	-
2.	1	1	0	6.71	93.29	1.969	0.826
3.	2	1.414	0.3	9.83	90.17	1.956	0.992
4.	3	1.732	0.47	15.67	84.33	1.925	1.195
5.	4	2	0.6	23.14	76.86	1.885	1.364
6.	5	2.236	0.69	28.79	71.21	1.852	1.459
7.	6	2.449	0.77	31.48	68.52	1.835	1.498
8.	7	2.645	0.84	50.69	49.31	1.692	1.704
9.	8	2.828	0.9	53.68	46.32	1.665	1.729

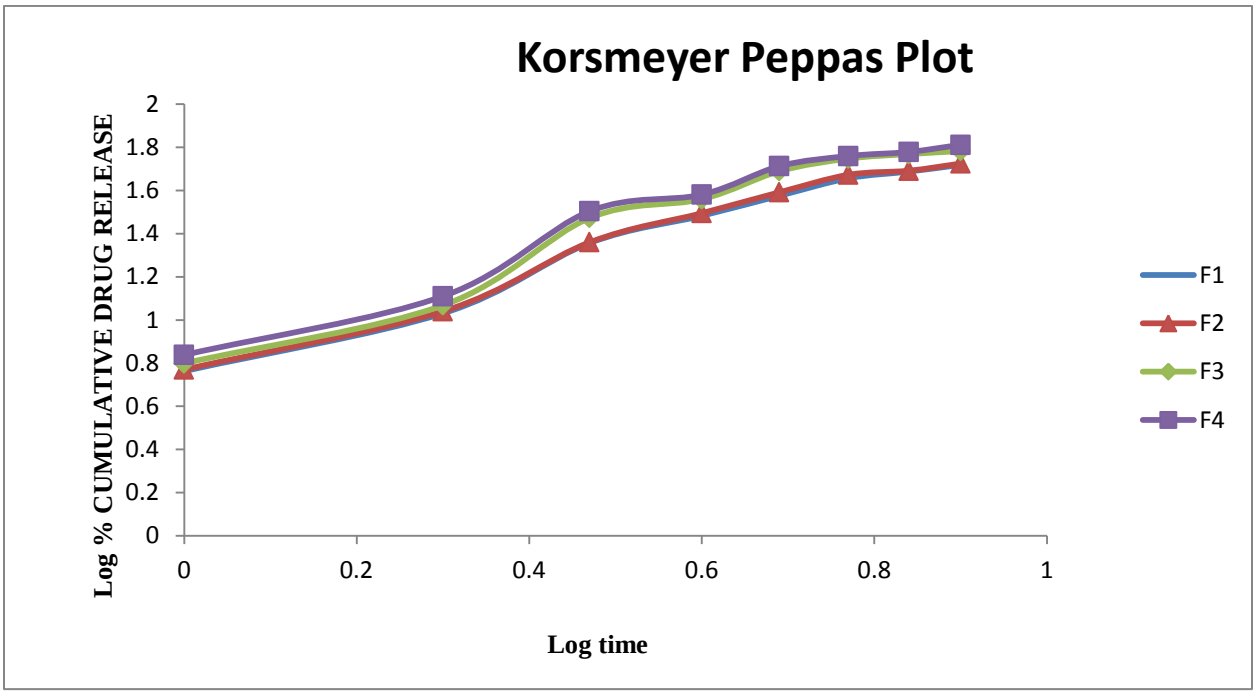
Graph no. 1 : Comparison of in vitro release of ketaconazole emulsion(zero order plot)



Graph no.2: Comparison of in vitro release of ketaconazole emulsion (first order plot)



Graph no. 3 : comparison of in vitro release of ketaconazole (highuchi plot)



Graph no. 4: comparison of in vitro release of ketaconazole (korsmeyer peppas)

Mathematical modeling: Data obtained from in-vitro permeation studies was treated by various conventional mathematical models to determine the release mechanism. Selection of a suitable release models was based on the value of R^2.

The regression coefficient of all four formulation are shown in table no. 5.16 and it was found that all the formulation follows the first order kinetics. The regression co-efficient for all formulations of highuchi plot was found to be almost linear.

Table no. 16: Model fitting release profile of Formulation F1 to F4

Formulation code	Zero order	First order	Higuchi model	Korsmeyer pepaas
F1	0.991	0.785	0.991	0.8573
F2	0.9762	0.9054	0.9762	0.928
F3	0.9491	0.9462	0.9491	0.959
F4	0.9615	0.9171	0.9615	0.9667

CONCLUSION

SEDDS formulation can be optimized for the deliverance of hydrophobic compounds with drug loading lowest amount of surfactant concentration and proper infinite dilution can be achieved without drug precipitation. Self-emulsifying drug delivery system may be apply for the formulations of drugs compounds with poor aqueous steadiness. Enlargement of this technology

SEDDS will continue to permit novel applications in drug delivery system. SEDDS has been exposed to be reasonably successful in improving the oral bioavailability of poorly water-soluble and Traditional research of SEDDS involves dissolution of drugs in oils and their blending with appropriate solubilizing agents.

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