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FORMULATION AND EVALUATION OF EMULGEL CONTAINING *PIPER NIGRUM* AND *CURCUMA LONGA* EXTRACT FOR VITILIGO.

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ABSTRACT

Vitiligo also known as leukoderma is a pigmentation disorder in which melanocytes in the skin are destroyed, white patches appear on the skin on various parts of the body. Present treatments such as UV radiation and corticosteroids have numerous side effects. The potency of Piperine and Curcumin as anti vitiligo were identified and an attempt was made to take this scope of piperine and curcumin in the treatment of vitiligo by formulating an effective topical emulgel so that side effects can be avoided, patient compliance can be achieved. In the treatment of vitiligo, an attempt was made to formulate and evaluate emulgel for the successful drug delivery in the treatment of vitiligo Formulated the *Piper nigrum* and *Curcuma longa* extract into an emulgel. Three types of gelling agents were used to prepare emulgel formulations: Carbopol 934, Carbopol 940 and HPMC K4M by dispersion in oil/ water emulsion based method. The effect of the type of the gelling agent on the releaseof drugs from the prepared emulgel has been investigated. The prepared emulgel were evaluated for physical parameters, drug content, pH, viscosity, extrudability, spread ability, etc. The studies of *In-vitro* drug release were conducted using Franz- Diffusion cell. The pH of all formulations was found to be in range of 6.0 -6.51 (near skin pH value).By using UV-Visible spectrophotometer the maximum wavelength of piperine and curcumin were determined using methanol and were found to be 341 and 421 nm respectively. Emulgel was formulated using light liquid paraffin as oil phase and emulsifying agent tween 80 for emulsion and incorporated into gel using different types of gelling agent. In prepared formulations the drug content of piperine and curcumin were determined and found to be in range of 78.10-80.50 % and 80.65-85.45%w/wrespectively. The in vitro drug release of all the formulations were determined up to four hours and maximum percent drug release of piperine (74.23%) and curcumin (79.05%) was shown by F4 and least percentage of drug release of piperine (70%) and curcumin (71.89)% was shown by F5.It was finally concluded that the formulation F4 with 1%w/w Carbopol 934 was found to be more promising formulations as it shows better physicochemical characteristics and drug release compared to other formulations. It was observed that the formulation was stable, which could increase the drug permeability across the skin and fast release of drug could be successfully achieved.

INTRODUCTION

Vitiligo is a chronic skin condition also known as leukoderma. This is caused by the pigment loss, which results in irregular pale patches of the skin. Vitiligo is a disorder in which the immune system targets the body's own pigment cells and tissues, melanocytes (autoimmune) in various parts of the skin. In affected areas, the pigment gradually disappears. [1]Our aim is to develop a topical dosage form of a suitable antivitiligo agent for the treatment of vitiligo. Medical treatments target the immune system, and trying to reverse the damage. The goal is to

restore the color of the skin by restoring healthy melanocytes to the area affected.Several therapies have been used to cure vitiligo such as the use of steroid creams, PUVA (psoralen and ultraviolet A light), narrow band UVB (ultraviolet B), various surgical procedures, analogs of vitamin D and pseudocatalase. These therapies are prone to undesired side effects while other herbal and natural remedies work without side effects against the immune system. [2]Topical drug delivery is an attractive route for both local and systemic treatment. Major drawback of topical dosage form in the delivery of hydrophobic drugs is dissolution and diffusion of drugs,and permeation through stratum corneum is for hydrophilic drugs. Therefore, to overcome this limitation, Emulgel are prepared. [3] As the name suggest, Emulgel is a combination of gel and emulsion. Both oil-in-water and water-in-oil form of emulsion used as a vehicle to deliver various drugs to the skin. Emulgel shows high ability to penetrate the skin. The presence of the gelling agent in water phase converts an emulsion into an emulgel. Emulsified gels are stable and better vehicle for hydrophobic or poorly water soluble drugs.Emulgel has dual release control system i.e. gel and emulsion. [4]Piperine, a commonly used kitchen spice, is the main constituent of pepperand has been reported to have various pharmacological activities.To exhibit a set of bioactivities, the structural features, an aromatic ring with a bridge of methylenedioxy, a conjugated dienone system and a piperidine ring constituting an amide bond, possessed by the molecule were considered important. Piperineis an alkaloid has the repigmentation capacity. In Vitiligo, the use of Piperine not only reduces UV radiation but also prevents side effects. Piperine not only stimulates the replication of melanocytes but also induces the formation of melanocytes dendrites. Phenolic amides from piperine also exhibited a superior antioxidant capacity than synthetic compounds. It can stimulate melanocyte proliferation and facilitates the re-pigmentation of de-pigmented skin.[5] Curcumin in turmeric is a hydrophobic polyphenol, one of the most powerful natural anti-inflammatory compounds.Curcumin helps in repairing skin. This property may help in the repigmentation in skin Due to its potent anti-oxidant and anti-inflammatory properties.

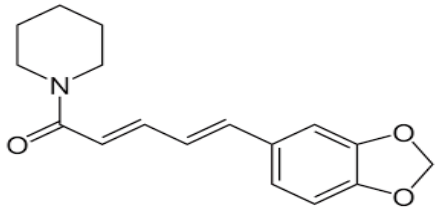

Figure 1: Structure of Piperine.

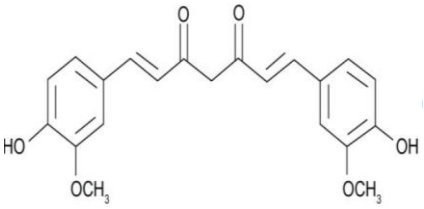

Figure 2: Structure of Curcumin

Turmeric can prove beneficial in manage of chronic skin issues of vitiligo. [6-7]Curcumin in turmeric is a potent natural immunomodulator. It modifies the immune system response to reduce inflammation and control the symptoms of vitiligo in a natural way. As a novel approach, in our investigation the topical emulgel is considered as a great potential product for an effective and safe way to administer both Piperine and Curcumin for the treatment of vitiligo. Compositions comprising Piperine and Curcumin which are able to stimulate the proliferation of melanocytes without significant adverse side effects have been used in present work for the treatment of vitiligo.Combining the Piperine in black pepper with Curcumin in turmeric shows synergistic effect. Rationale of the work is to provide stable and better vehicles for hydrophobic or poorly water soluble drugs by formulating emulgel containing Piperine and Curcumin combination. It will be able to localize the drugs in the dermis by penetrating through stratum corneum. Piperine and Curcumin both are hydrophobic in nature hence it becomes difficult to incorporate these drugs in gel or hydrogels. To solve this problem emulgel approach can be advantageous. The proposed research work will be an attempt to incorporate black pepper and turmeric extract in an emulsion and formulation of a topical emulgel. Certain oils like Coconut oil can be used in oil phase which may offer additional advantage to the vitiligo therapy.

Coconut oil helps a lot in curing vitiligo. Coconut oil helps in the repigmentation of the skin. It covers the pigment loss from the skin and leads to increased melanocyte production in the skin. [8]

MATERIAL AND METHODS:

Materials:

Piperine and Curcumin were obtained as a gift sample from SV Agrofood, Navi Mumbai, India. The excipients used were of standard pharmaceutical grade and all chemicals and reagents used were of analytical grade.

Method:

Preparation of Emulgel[9]

Preparation of emulgel incorporates three stages:

Different formulations were prepared using different types of gelling agent. The method only varies in the process of making gel in different formulations. The method of emulsion preparation was same in all the formulations.

Step 1: **Formulation of emulsion (O/W type):** Oil phaseof the emulsion was made by dissolving emulsifier e.g. Span 80 in oil vehicle (light liquid paraffin) while the aqueous phase is made by dissolving hydrophilic emulsifier (Tween 80) in purified water. Added substances like methyl paraben and propyl paraben are separated in humectant like propylene glycol and mixed with the drug extracts were dissolved in ethanol, being hydrophobic was dissolved in oil phase. Ethanol acts as a cosolvent for the drug while propylene glycol was used as a cosolvent as well as humectant. Coconut oil was also mixed in oil phase. Both the oily and aqueous phases were heated separately to 70-80 ° C; the oily phase was then added with continuous blending into the aqueous phase. This mix was cooled to room temperature to get an emulsion.**Step 2: Formulation of gel base:** The gel bases were prepared by dissolving Carbopol 934 and Carbopol 940 in distilled water separately with constant stirring at a moderate speed using mechanical shaker. Formulations F1 –F4 were prepared by Carbopol 934 and F5 by Carbopol 940 as gelling agent. F6 was prepared by dispersing HPMC K4M in heated distilled water (80° C),and dispersion was cooled and left overnight and the pH was adjusted to 6-6.5 with triethanolamine.

Step 3: Incorporation of emulsion into gel base with steady blending:The emulsion was mixed into the gel in 1:1 ratio to obtain emulgel.

EVALUATION OF EMULGEL:

Physical examination: Visual inspection of the formulated emulgel for their color, homogeneity, consistency and phase separation have been carried out.

Determination of pH:[10]By using digital pH meter the pH of the formulation was determined. pH meter electrode was washed with distilled water and then dipped into the formulation to measure pH and repeated this process 3 times.

Spreadability measurement [11]The Spreadability of various emulgel formulations were evaluated by compressing the sample under several glass plates of known weight. Twenty glass plates were subsequently placed over the sample at 1-min intervals. In the vertical and horizontal axes, the spreading areas reached by the sample were measured in millimeters. The results were expressed in terms of the spreading area as a function of the applied weight according to the following equation:

$$Si = d^2 \times \pi/4$$

In which *Si* is the spreading area (mm^2) resulting from the applied weight*i*(g), and *d* is the mean diameter (mm) that the sample has reached. To obtain the spreading profiles, the spreading area was plotted against the plate weight.

Extrudability: [12] The Extrudability of emulgel was determined by using aluminum collapsible tubes filled with 10 gms emulgel and sealed by crimping to the end. The weights of the tubes were recorded by weighing. The Tubes were placed and clamped between two glass slides. A tube was compressed by placing 500 gm weight over the slides and cap was removed. The extrudability of the emulgel was calculated in terms of weight in grams required to extrude a 0.5cm ribbon of gel in 10 seconds.

Extrudability = Weight applied to expel emulgel from tube (in gm)/ Area (in cm^2)

Viscosity Studies: Viscosity of the emulgel was measured using Brookfield viscometer. Spindle type; model LVDV-E at 60 rpm. In a beaker 200 grams of the gel was taken and the spindle was dipped in it for about 5 minutes and then the reading was taken.

Table 1:Composition of different formulation batches (%w/w)

Ingredients	Batches					
	F1	F2	F3	F4	F5	F6
Piperine	1	1	1	1	1	1
Curcumin	1	2	3	4	4	4
Carbopol 934	1	1	1	1	-	-
Carbopol 940	-	-	-	-	1	-
HPMC K4M	-	-	-	-	-	1
Liquid paraffin	7.5	7.5	7.5	7.5	7.5	7.5
Tween 80	0.5	0.5	0.5	0.5	0.5	0.5
Span 80	1	1	1	1	1	1
Propylene glycol	5	5	5	5	5	5
Ethanol	2.5	2.5	2.5	2.5	2.5	2.5
Coconut oil	1	1	1	1	1	1
Methyl paraben	0.03	0.03	0.03	0.03	0.03	0.03
Propyl paraben	0.01	0.01	0.01	0.01	0.01	0.01
Triethanolamine	q.s	q.s	q.s	q.s	q.s	q.s
Purified water (ml) q.s to	100	100	100	100	100	100

Analytical Methods:

Selection of common solvent: [13] After the solubility study of both drugs in different solvent, methanol was confirmed as a common solvent for developing spectral characteristic.

Preparation of Standard stock solution of Piperine and Curcumin [14] The stock solution (100µg/mL) of Piperine and Curcumin were prepared by dissolving accurately about 10 mg of each drug in sufficient quantity of methanol and then volume was adjusted to 100 ml with methanol. Further series of dilutions were made with methanol.

Determination of λmax[15] Solutions of Curcumin (10 µg/mL) and Piperine (10 µg/mL) prepared in methanol was subjected to overlay scan in a UV spectrophotometer from 200-600 nm. It was confirmed that λmaxfor Curcumin and Piperine are of 421 and 341 nm, respectively.

Calibration curve of Piperine and Curcumin[16-18] A calibrated volumetric flask of 10 ml were taken in a series and appropriate aliquots of the working standard solution of piperine were withdrawn and diluted with methanol up to 10 ml. The absorbance was measured against the reagent blank prepared in similar manner without piperine at absorption maxima of 341 nm. The Same procedure for curcumin was applied and absorbance was measured at 421 nm, against the reagent blank prepared in similar manner Without curcumin. There was a graphical presentation of the linear correlation between the concentration (x-axis) and absorbance (y-axis). Slope (m), intercept (b) and correlation coefficient (R2) were calculated from the linear equation (Y= mx + b) by regression.

Simultaneous Equation Method

From the overlain spectra (shown in figure 6) of Piperine (10 µg/ml), Curcumin (10 µg/ml) and the mixture of piperine-curcumin solution (10 µg/ml of each), two wavelengths i.e. 341nm as λmax of Piperine and 421nm as λ max of Curcumin were selected as the working wavelength, at which both drugs showed absorbance for each other. The absorptivity of these two drugs was determined at 341nm and 421nm.At selected wavelength a set of two simultaneous equations were formed using the absorptivity values as given below.The concentrations of two drugs piperine and curcumin in mixture were calculated using set of two simultaneous equations.

$$C_X = \frac{A2\ ay1 - A1\ ay2}{Ax2\ ay1 - ax1\ ay1}$$

$$Cy = \frac{A1\ ax2 - A2\ ax1}{Ax2\ ay1 - ax1\ ay1}$$

Where, Cx and Cy are concentrations of Piperine and Curcumin in µg/mL respectively in known sample solution. A1 and A2 are absorbances of sample solutions at 341nm and

421nm respectively. ax1 and ax2 are absorptivity of Piperine at 341 nm and 421 nm, ay1 and ay2 are absorptivity of Curcumin at 341 nm and 421 nm.The concentration of Cx and Cy in emulgel formulation can be obtained by solving equation (1) and (2).

Determination of Absorptivity Value.[19]

The absorptivity value of Piperine and Curcumin from each solution was calculated using following formula.

$$\text{Absorptivity} = \frac{\text{Absorbance}}{\text{Concentration}} \text{ (gm/100 mL).}$$

Drug content determination:[20]By dissolving a known weight (0.1 gram) of the emulgel formulation in 10 ml methanol, the drug content of emulgel was determined, appropriate dilutions were made and then filtered the resulting solution to obtain clear solution.Absorbances of Piperine and Curcumin were measured at 341nm and 421 nm respectively by using UV spectrophotometer. Drug content of both Piperine and Curcumin in emulgel formulations were determined by using simultaneous equation.

Ex-vivo permeation studies[21]

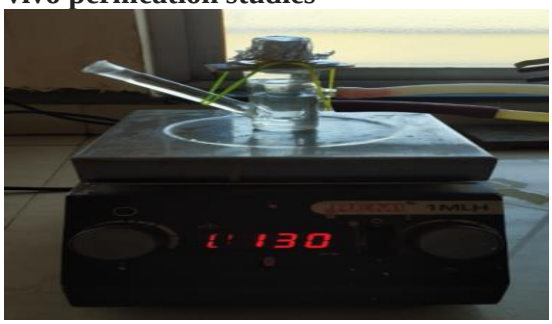

Figure 3: Ex-vivo permeation studies using human cadaver skin (Franz diffusion cell apparatus)

Ex-vivo permeation studies were conducted using human cadaver skin of 2.5 cm * 2.5 cm. Hair on the cadaver skin was shaved using a hand razor and adhering subcutaneous fat was carefully cleaned. A Franz's diffusion cell apparatus with a diameter of 25 mm and a diffusional area of 2.83 cm^2 was used for permeation studies. Pretreated cadaver skin was set in place with the stratum corneum facing the donor compartment and the dermis facing the receptor compartment in the Franz diffusion as shown in fig. 3. The receptor compartment was filled with 20 ml of phosphate buffer 6.8. 1 gm of emulgel was spread over an area of 1 cm^2 to the skin membrane and placed across the donor compartment. The temperature of the diffusion medium was maintained at 37 ± 2 °C and stirred at 100 rpm. Samples (2 ml) was withdrawn for 0, 15, 30, 45, 60, 90, 120, 180 and 240 min and replaced with an equal volume of fresh buffer to maintain sink conditions. Samples were analyzed spectrophotometrically for drug content of Piperine and Curcumin at 341 nm and 421 nm respectively.

1) FT-IR Spectroscopic Study:[22]

The compatibility studies were carried out at room temperature using FTIR spectroscopy to determine the drug-drug interaction, drug-excipients/polymer interactions used in the formulations. The incompatibility between the drug and, excipients can alter the physicochemical and therapeutic properties of the drug molecule and hence can have an impact on the dosage form effectiveness, safety profile, and stability. Therefore, drug- excipient interaction study at the preliminary stage of a formulation development should be considered as an important step to confirm the correct choice of excipients, hereby, increasing the likelihood of developing a stable and effective dosage form.

RESULTS AND DISCUSSION:

Physical Appearance:

Emulgel formulations were yellow viscous creamy preparation with a smooth homogeneous texture and glossy appearance. Results have been discussed in **Table 2.**

pH Determination:

pH of Prepared Emulgel were measured by using digital pH meter. The pH of the emulgel formulation was in the range of 6.0-6.51 which meets the pH of the skin and considered acceptable to avoid the risk of skin irritation upon application to skin.

Spreadability measurement:

The Spreadability of various emulgel formulations are given below in **Table 4**. It was concluded that all the prepared formulation showed acceptable Spreadability. The value of Spreadability indicates the degree of shear required to apply the emulgel.

Extrudability:

Extrudability of all the emulgel formulations was higher than 80%. Therefore, it can be said

that extrudabilty of the all formulations shows good properties of acceptance

Viscosity Studies:

The tests were performed by using Brook-field Viscometer. As the polymer type changes, the viscosity of formulations also get changes. When batches F1, F2,F3,F4 are compared with F5, F6 it can be seen that batches made using Carbopol 940 are much viscous than that of the batches made using Carbopol 934 and HPMC K4M. Results are given in **Table 6.**

Analytical Methods:

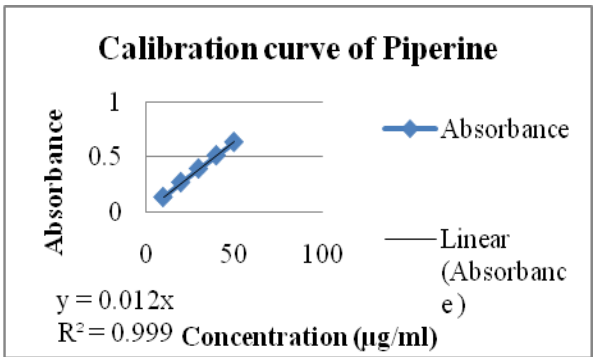

Figure 4: Calibration curve of Piperine in Methanol at 341 nm.

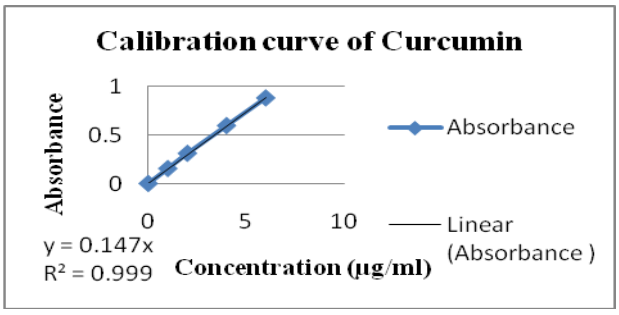

Figure 5: Calibration curve of Curcumin in Methanol at 421 nm.

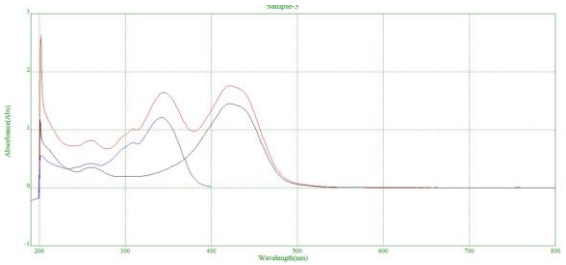

Figure 6: Overlain spectra of Piperine (A), Curcumin (B) and Mixture (C) on U.V. spectrophotometer

Drug Content determination:

The drug content of all prepared emulgel formulations were estimated by using UV Spectrophotometer using simultaneous equation. The F4batch shows maximum and F1 batch shows minimum % of drug content. Determination of the drug content showed that the drug was uniformly distributed throughout the emulgel.

Ex-vivo permeation studies: The *In-vitro* release profile of different formulations of emulgel is shown in Fig.3. It was observed that all formulations of emulgel showed better release of drugs. In case of Carbopol 934 based formulations the release of the drug can be ranked in the following descending order: F4 > F3 > F2> F1, Where the amounts of the drug release of piperine and curcumin after 4 hrs. were 72.35%, 72.58%, 73.01%, 74.23% and 74.57%, 76.68%, 78.19%, 79.05% respectively while in case of Carbopol 940 (F5) and HPMC K4M (F6) based formulation, Where the amounts of the drug release of piperine and curcumin after 4 hrs. were 70.0%, 72.5% and 71.89%, 72.35% respectively. From these results it can be concluded that Carbopol 934 based formulations show higher drug release in comparison with Carbopol 940 and HPMC K4M based formulations. The lower drug release from F5, which is Carbopol 940-based, than the drug release from F1 – F4, which is Carbopol 934-based, this may be due to the higher viscosity of Carbopol 940 emulgel formulation.

FTIR study was done to assess the compatibility amongst the drug and other formulation excipients. FTIR technique is used to investigate the interaction arising between the drug as well as excipients by comparing the peaks of the spectra. Shifting or disappearance of the existing peak and appearance of new peaks are considered as an indication of interaction.

Table 2: Physical parameter of formulation batches.

Formulatio	Color	Homogeneity	Consistency	Phase separation
F1	Light Yellow	Excellent	Excellent	None
F2	Light Yellow	Excellent	Excellent	None
F3	Yellow	Excellent	Excellent	None
F4	Yellow	Excellent	Excellent	None
F5	Yellow	Excellent	Excellent	None
F6	Yellow	Excellent	Excellent	None

Table 3: pH of emulgel formulation

Formulation	F1	F2	F3	F4	F5	F6
pH	6.0	6.19	6.23	6.4	6.45	6.51

Table 4: Spreading coefficient of the formulation F1–F6

Formulation Code	F1	F2	F3	F4	F5	F6
Spreadability (mm)	15.73	16.47	18.53	20.11	13.34	14.95

Table 5: Extrudability of all formulations

Batches	Weight of emulgel in tube (gm)	Weight of emulgel extruded	Extruded amount (%)
F1	9.98	8.67	86.87
F2	9.88	8.61	87.14
F3	9.76	8.39	85.96
F4	10.04	8.92	88.84
F5	10	8.26	82.6
F6	10.07	8.52	84.60

Table 6: Viscosity studies of all emulgel formulations

Batch	Viscosity (cps)
F1	7450
F2	8300
F3	9700
F4	9850
F5	16882
F6	4382

Table 7: Drug content of all Emulgel Formulations.

Formulation Code	Drug Content (%)	
	Piperine	Curcumin
F1	78.10	80.65
F2	78.90	82.45
F3	79.00	84.43
F4	80.50	85.45
F5	79.30	81.66
F6	78.70	80.78

Table 8: *In-vitro*% cumulative Drug Release Data for F1-F6.

Time (min)	% Cumulative Drug Release											
	F1		F2		F3		F4		F5		F6	
	P	C	P	C	P	C	P	C	P	C	P	C
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
15	6.54	7.93	5.87	8.60	6.47	8.67	6.78	11.20	5.25	8.09	6.78	6.87
30	8.25	10.43	8.09	10.85	8.24	19.23	8.95	14.29	7.46	12.02	8.67	15.44
45	15.24	16.47	12.53	18.80	16.30	24.31	16.07	23.34	14.10	20.87	15.44	22.67
60	19.25	25.15	18.27	26.47	18.87	32.12	19.74	32.40	18.40	31.07	19.13	35.42
90	30.47	37.83	29.12	35.61	31.42	49.36	32.16	40.59	29.25	38.01	30.45	41.32
120	43.90	46.31	43.88	48.76	42.12	62.21	46.13	53.24	42.03	48.32	42.35	58.34
180	50.82	59.93	50.24	62.23	57.25	69.34	51.24	65.68	48.76	62.95	49.67	65.78
240	72.35	74.57	72.58	76.68	73.01	78.19	74.23	79.05	70	71.89	72.5	72.35

P=Piperine C=Curcumin

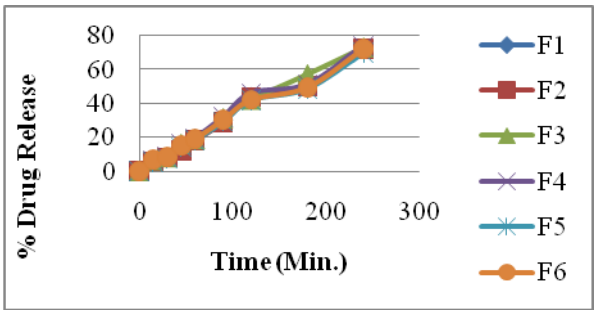

Fig. 7: % Drug Release of Piperine of F1 to F1 to F6 Formulations

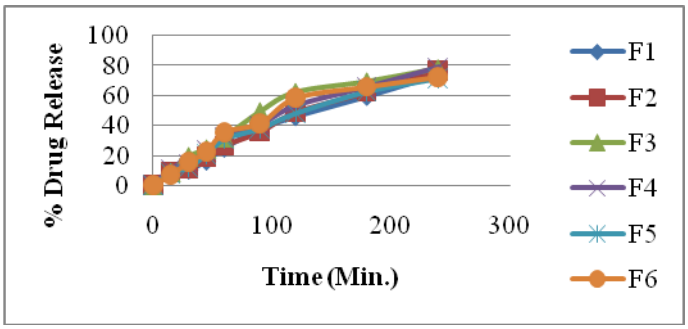

Fig. 8: % Drug Release of Curcumin of F1 to F6 Formulations

FT-IR Spectroscopy Study:

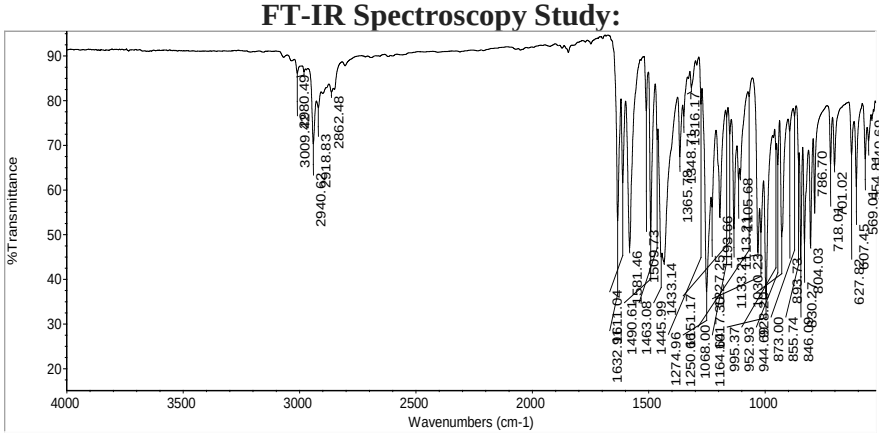

Figure 9: FTIR Spectra of Piperine pure drug

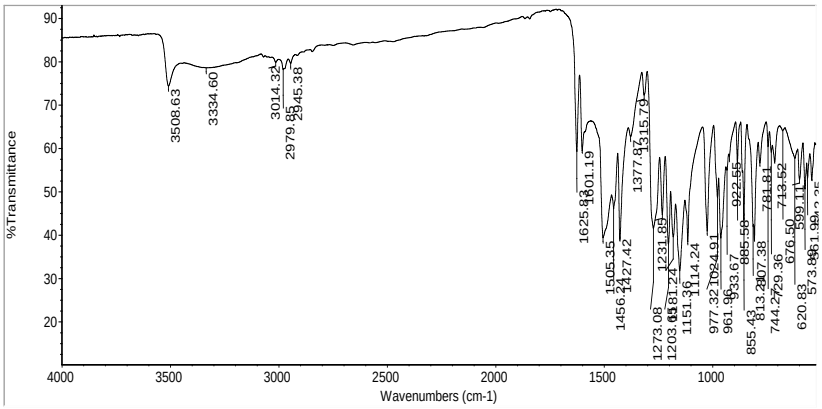

Figure 10: FTIR Spectra of Curcumin pure drug

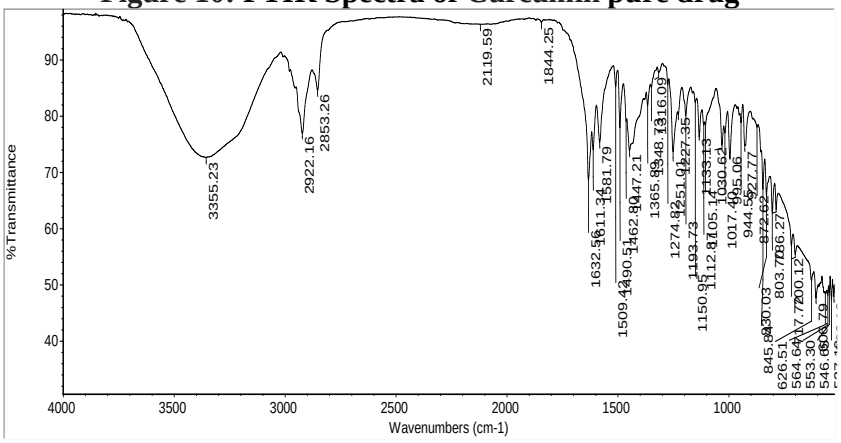

Figure 11: FTIR Spectra of Piperine, Curcuminand Excipients.

The FTIR study was done for formulation F4.

Functional groups	Wave number of pure piperine drug	Wave number of Piperine in its emulgel formulation
Unsaturation (alkenes)	3009.42	3355.23
CH_2	2918.83	2922.16
C=O stretching	1632.91	1632.56
C-C-O	1250.66	1251.01
Ketonic group	1581.46	1581.79
C-N stretching	1030.23	1030.62

Table 9: Interpretation of FTIR spectra of piperine and its emulgel formulation

Functional groups	Wave number of Pure Curcumin	Wave number of Curcumin in its Emulgel Formulation (nm)
Stretching vibration of the phenolic –OH group and conjugated ketonic –C=O vibrations.	3508.63	3355.23
Ar, C-H	2979.85	2922.16
C=O	1625.83	1632.56
Stretching –C=C vibrations of benzene, aromatic –C-O stretching of (-OMe and –OH), and –C-O-C stretching (-OMe)	1505.35	1509.42
	1273.08	1274.82
	1151.36	1150.95
C-O	1203.65	1227.35

The FTIR spectra of physical mixture exhibited all the distinguishing peaks of Curcumin, Piperine and other excipients with no significant peak shifting and disappearance of existing peaks indicating their compatibility. The FTIR spectrum shows that the peaks were not altered in the physical mixture of drugs with excipients used in formulation indicating that there were no interactions occurred between the drugs and excipients.

CONCLUSION: The aim of the study was to formulate and evaluate emulgel a topical dosage form of selected antivitiligo agents. The conventional treatments were followed by several unwanted side effects. The Piperine and Curcumin extract was formulated into 6 different emulgel formulations by using different polymers like Carbopol 934, Carbopol 940 and HPMC K4M. The pH of all the formulations were found to be 6.0 to 6.51 and drug content of Piperine and Curcumin were determined and found to be in range of 78.10-80.50 % and 80.65-85.45% w/w respectively.In terms of Gel Consistency, Viscosity, Spreadability and Extrudability, F4 (1 % Carbopol 934) was found to be optimum on physical evaluation of all formulations. The *In-vitro* release studies were conducted and results are shown in Tables 8 and graphs shown in fig. 7-8. F4 formulation showed the highest drug release of Piperine (74.23%) and Curcumin (79.05%) in 240 min. FTIR studies showed the compatibility between drug, excipients, and Carbopol. Combining the Piperine in black pepper with Curcumin in turmeric shows synergistic effect. Rationale of the work is to provide stable and better vehicles for hydrophobic or poorly water soluble drugs by formulating emulgel containing Piperine and Curcumin combination. It will be able to localize the drugs in the dermis by penetrating through stratum corneum. Piperine and Curcumin both are hydrophobic in nature hence it becomes difficult to incorporate these drugs in gel or hydrogels. To solve this problem emulgel approach can be advantageous. Emulsion system provides solubalisation of hydrophobic drugs, thus imparts in enhancing availability of drug in the formulation. This dosage form imparts great patient compliance. Emulgel will act as drug depot that releases drug in sustained manner. Hence the optimized formulation may be used to treat the topical skin diseases (vitiligo).

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