ejpmr, 2023, 10(5), 374-386

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

FORMULATION AND EVALUATION OF EMULGEL CONTAINING LIQUORICE EXTRACT

***Neethu Sreejan and Dr. Suja C.**

Department of Pharmaceutics,Crescent college of Pharmaceutical Sciences,Payangadi P O Kannur- 670358.

***Corresponding Author: Neethu Sreejan**

Department of Pharmaceutics,Crescent college of Pharmaceutical Sciences,Payangadi P O Kannur- 670358.

Article Received on 13/03/2023 **Article Revised on 02/04/2023** **Article Accepted on 23/04/2023**

ABSTRACT

Emulgel is one of the most important topical drug delivery system as it has double release control system i.e emulsion and gel. The emulsion is incorporated into the gel matrix to prepare emulgel which forms a viscous formulation and provides better permeation and stability. The aim of this study is to formulate emulgels containing Liquorice extract and evaluate the formulations for better and improved therapeutic activity. Hydrophilic and hydrophobic drugs can be easily incorporated in nano-emulsion and stability can be enhanced with the help of a gelling agent. Formulations were prepared using different concentrations of oil phase (liquid paraffin), surfactant (tween 80) and (PEG 400)as co-surfactant by spontaneous emulsification method. Region of nano-emulsion system was found in the pseudo-ternary phase diagrams developed at different ratios of surfactant and oil. Nano-emulgels loaded with drugs were characterized for, viscosity, spreadability, particle size, zeta potential, *in-vitro* drug release, anti-microbial and anti-inflammatory studies. The optimized formulation, F4 showed a drug release of 94% at the end of 6 hours & followed zero order kinetics with non fickian release pattern. The result showed that the liquorice extract was loaded in water in oil type of emulsion and was found to be homogenous,and the in-vitro release study shows that F4 formulation shows the maximum drug release. As it combines the advantage of an emulsion and gel it can be concluded that liquorice extract of nano-emulgel can be effectively used as a topical dosage form.

KEYWORDS: Nanoemulsion, Liquorice Extract, Nanoemulgel.

INTRODUCTION

Topical drug delivery can be defined as the application of a drug containing formulation to the skin to treat cutaneous disorder directly. It is the simplest and easiest route of localised drug delivery anywhere in the body by various routes such as ophthalmic, rectal, vaginal and skin. Skin is one of the most readily accessible parts of human body for topical administration and molecules penetrate in the skin.The rate of drug release from a topical preparation is dependent directly on the physiological features of the carrier. Drugs are administered topically for their action at the site of application or for systemic effects. Topical formulations are prepared in different consistency such as solid, semisolid, and liquid.A technique such as emulgel can aid in the easy penetration of the drug into the skin and provide a rapid onset of action.[1]

EMULSION

Emulsions are made by combining two or more liquids that are normally incompatible. In this system, the oil phase is made miscible with the aqueous phase using an emulsifying agent. The use of emulsifying agents helps to stabilize emulsions. They are easy to wash off and they also penetrate well.

Types of emulsion include;

- **Microemulsion** – Microemulsions are isotropic mixtures of a biphasic o/w systemic stabilized with a surfactant that is thermodynamically stable and optically clear. Droplets vary in size from 10 to 100nm and do not coalesce.
- **Nano-emulsion** – Nanoemulsion is transparent (translucent) oil-water dispersions that are thermodynamically stable due to surfactant and cosurfactant molecules with a globule size range from 1nm to100 nm.
- **Macroemulsion** – Emulgel with emulsion droplet particle sizes greater than 400nm. They are physically invisible, but under a microscope, the individual droplets can be seen clearly.

GEL

A gel is made up of a polymer that enlarges when exposed to fluid and possibly within its structure. The amount of fluid entrapped in the gel determines its rigidity. These gels are wet and smooth, with the

appearance of being solid and it also enhance the viscosity of liquid preparation.Gels can be used as a thickening agent and also help to improve the homogeneity and consistency of a formulation. This agent is used to create a gel base, which is then mixed with emulsion to create emulgel.

EMULGEL

Emulgel is known as an emulsion that has been gelled by using a gelling agent. They can be made either o/w or w/o type. Both hydrophobic and hydrophilic drugs drugs can be easily incorporated into the emulsion and the stability can be enhanced with the help of a gelling agent.In recent years, they have been used as a control release formulation. These are biphasic systems that have better drug loading capacity and better stability.

On the other hand there is a growing demand in industry for plants used in traditional medicine, *Glycirrhiza glabra* belonging to the family fabaceae.The term *liquorice* originated from the Greek word *glykosrhiza* in which *glykos* means "sweet" and *rhiza* means "root. The rhizome and root of *G. glabra* have been used for different medicinal and economical purposes. They have various applications in cosmetics, medicine, and pharmaceutical industries, and are used in confectionary, food, and tobacco industries as a sweetener. contains varieties of phytoconstituents such as saponins (mainly glycyrrhizin), flavonoids (mainly liquiritigenin and liquiritin), isoflavons (mainly glabridin, coumarins, stilbenoids), and miscellaneous compounds. This study was planned to formulate emulgels containing liquorice extract and evaluate the formulation for better and improved anti-bacterial and anti-inflammatory activity of the developed formulation.

1. MATERIALS AND METHODS

1.1 Chemicals used

Liquorice (Yucca Enterprises,Mumbai) and it was authenticated from MVR Ayurveda Medical Centre-Parassinikadav, Tween 80(Burogyne Burdidges and co, Mumbai), Liquid Paraffin, PEG 400, and carbopol 940.

1.2 Instruments used

Double beam UV spectrometer, FTIR (Bruker Alpha-Attenuated Total Reflectance FTIR), Digital Ph meter(Roy Instruments Varanasi), Brookfield viscometer(LVDV Prime-1), Malvern Nano-zetasizer Zs90(Malern).

1.3 EXTRACTION OF LIQUORICE ROOT

Liquorice root was pulverized into fine powder. The dried powder (100g) was soaked in one liter of 70% ethanol for two days for softening which enhances the extraction process. To accelerate the extraction process, the liquorice powder in alcohol mixture was blended using an mixer for 10 minutes at room temperature, then the resulting extract was filtered through folded gauze and filtered again using Whatman filter papers. The filtrate was poured in glass petri dishes for evaporation in air to give a residue which will then be scratched, weighed and kept in an airtight closed container.[3]

EXTRACTION OF GLYCIRRHIZIN

Liquorice root powder was macer-ated with the solvent mixture of acetone and dilute nitric acid for 2 h. The contents were filtered and additional 20 ml of acetone was added to the marc and warmed gently. The contents were filltered and filltrate was obtained. To this Fltrate sufficient volume of dilute ammonia solution was added till precipitation of ammonium glycyrrhizinate is completed. The precipitate was collected and washed with 5 ml of acetone, dried and collected.

1.4 Phytochemical Screening

Phytochemicals are non-nutritive plant chemicals that contain protective, disease-preventing compounds. Standard screening test were carried out for the extracted product. Extract were screened for presence or absence of secondary metabolites such as carbohydrates, tannins flavonoids, saponins and glycosides using standard procedures to identify the constituents.

1.4.1 Test for carbohydrates

A small quantity of extract was dissolved in 4ml of double distilled water and filtered. The filtrate was subjected to molisch's test to detect the presence of carbohydrates and further add Fehling's reagent to it. If it shows brick red colour,the presence of reducing sugar can be confirmed.[2]

1.4.2. Test for Glycosides (Keller-Killani test

A portion of liquorice extract is mixed with glacial acetic acid, few drops of ferric chloride and concentrated sulphuric acid are added,and observed for reddish brown colouration at the junction of two layers confirms the presence of glycosides.[2]

1.4.3. Test for Saponins (Froth test)

About 0.5gm extract was dissolved in 10ml of distilled water for about 30 seconds. The test tube was stoppered and shaken vigorously for about 30 seconds. The test tube was allotted to stand in a vertical position and observed over 30 minutes period of time. If a honey comb froth is formed above the surface of the liquid persists after 30 mins then the sample is suspected to contain saponins.[2]

1.4.4. Test for Tannins (Ferric chloride test)

About 0.5g of liquorice extract were boiled in 20ml of distilled water in a test-tube and then filtered. A few drops of 0.1% ferric chloride added and observed for brownish or blue-black colouration.[2]

1.4.5 Test for Free Flavonoids

A portion of the powdered plant sample was heated with 10ml of ethyl acetate over a steam bath for 3min. the mixture was filtered and 4ml of the filtrate was shaken with 1ml of dilute ammonium solution. Yellow colour is observed if it shows the presence of flavanoids.[2]

1.5 Thin Layer Chromatography

For preparing test solution, alcohol and water (7:3) was mixed to liquorice extract. The solution was heated in water bath for 5 minutes, cooled and filtered. Developing solvent system contains the mixture of butyl alcohol, water and glacial acetic acid (7:2:1). TLC plates were prepared using silica gel solution and the retention value (Rf) was calculated. The plates were kept in developing solvent system and examined under UV light at 254nm.

1.6 Construction of Pseudo-Ternary Phase Diagram

To find the concentration range of ingredients,pseudo-ternary phase diagrams were constructed, using the water titration method .The mixtures of oil, S:Cos (Smix) at different ratios1:1,2:1,3:1 were diluted by adding water dropwise, under specific magnetic stirring. After being equilibrated, the mixtures were, assessed physically and determined as nanoemulsion.[4]

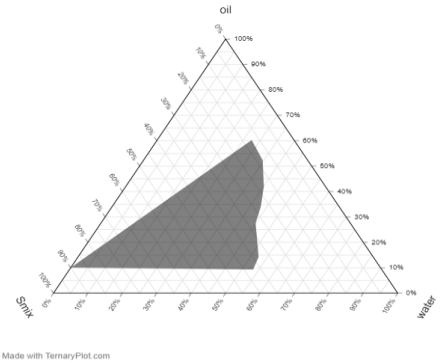


Fig no:1 Ternary diagram with Smix ratio 1:1

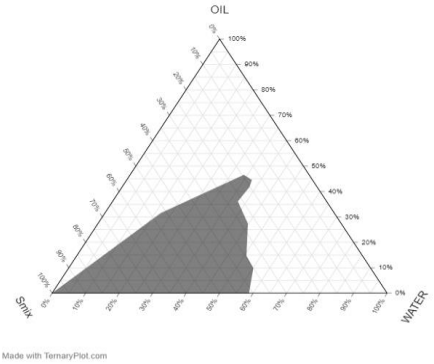


Fig no:2 Ternary diagram with Smix ratio 2:1

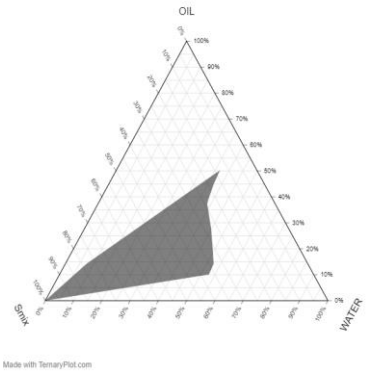


Fig no:3 Ternary diagram with Smix rati 3:1

1.4.7 Formulation of Liquorice Extract Loaded Nano-Emulsion

The preparation of nano-emulsion involves the construction of pseudo-ternary phase diagram composed of oil, water, surfactant and co-surfactant. The nano-emulsion was prepared by low energy emulsification method. The oil phase was prepared with liquid paraffin, tween 80 and PEG 400 were dissolved in distilled water(aqueous phase) and added to the clear oil phase, drop by drop.Water-in-oil (w/o) nanoemulsions were obtained under magnetic stirring at room temperature. Required quantity of drug was incorporated into it.[4]

Preparation of Carbopol gel

Carbopol gel is prepared by dispersing the Carbopol 940 (1 g) in a sufficient quantity of distilled water. After complete dispersion, the Carbopol 940 solution was kept in the dark for 24 hours for complete swelling and required quantity was incorporated into different formulations.

Table 1: Formulation of Liquorice Extract Emulgel.

FORMULATION CODE	LIQUORICE EXTRACT (g)	LIQUID PARAFFIN (OIL) (ml)	TWEEN 80 (SURFACTANT) (ml)	PEG 400 (CO-SURF) (ml)	Smix RATIO	WATER (ml)	CARBOPOL 932 (g)	METHYL PARABEN (mg)	TRIETHANOL-AMINE (ml)
F1	1	40	25	25	1:1	10	2.25	0.3	1
F2	1	35	23	23	1:1	19	2.25	0.3	1
F3	1	38	20	20	1:1	22	1.5	0.3	1
F4	1	32	30	15	2:1	23	3.5	0.3	1
F5	1	30	25	17.5	2:1	27.5	3	0.3	1
F6	1	35	32.5	12.5	2:1	20	1.5	0.3	1
F7	1	25	40	13.33	3:1	21.67	3.5	0.3	1
F8	1	30	36	12	3:1	22	2.25	0.3	1
F9	1	34	30	10	3:1	26	2.25	0.3	1

1.5 ANALYTICAL METHODS

1.5.1 Determination of lambda max

100mg of liquorice extract was dissolved in phosphate buffer 6.8 and diluted upto 100ml to get concentration of 1000ppm which is taken as the stock solution. The stock solution was further diluted to get different concentrations. Resultant solutions were scanned for max in the range of 200-400nm using UV spectrophotometer.

1.5.2 Preparation of standard calibration curve of liquorice extract

The standard stock solutions of liquorice extract was prepared by dissolving 10 mg of extract in Phosphate Buffer (pH6.8) : Ethanol in 70 : 30 proportion and final volume was adjusted with same solvent in 10mL of volumetric flask to get a solution containing 1000 µg/mL of liquorice extract. Aliquots of working stock solutions was prepared with in the same solvent to get concentration in range of 5-35µg/ml of glycyrrizin. The absorbance of resulting solutions was measured at 254nm.

1.6 Preformulation studies

Preformulation testing was an investigation of physical and chemical properties of a drug substance alone. It was the first step in rational development of dosage form.

1.6.1 Solubility studies

Solubility of liquorice extract was observed in different solvents such as distilled water, ethanol, phosphate buffer 6.8 and phosphate buffer 7.4.

1.6.2 Organoleptic properties

Physical appearance of the extract was observed.

1.6.3 Drug excipient interaction studies

FT-IR spectra of liquorice extract, carbopol, tween 80,liquid paraffin were taken by KBr pellet technique between 600-4000cm. This is to ensure that there is no incomptability between drug and gelling agents. Once spectra was recorded, the peaks of extract and, excipients were compared for incomptability.

1.7 Evaluation of liquorice extract emulgel

1.7.1 Physical Appearance

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

1.7.2 Rheological Studies

Viscosity (in Cps) of prepared emulgel formulationswere determined using Brookfield viscometer with spindle no. 63 at a speed of 50 rpm and this was repeated 3 times. The formulation whose viscosity was to be determined was added to the beaker and was allowed to settle down for 30 min at temperature (25o ±1oC) before the measurement was taken. Spindle was kept perpendicular into the centre of emulgel taking care that spindle does not touch bottom of the jar and rotated at a speed of 50 rpm for 10 min. The viscosity reading was noted.

1.7.3 pH determination

1g of emulgel was accurately weighed and dispersed in 100ml of distilled water and it is placed for 2 hours. The pH of dispersion was measured by using a digital pHmeter. The measurement of pH of each formulation swere done in triplicates and average values were calculated.[3]

1.7.4 Spreadability

Spreadability of formulation was determined by using an apparatus designed and developed in laboratory especially for project .Two rectangular glass plates of same dimension were selected. 0.5g of sample was placed on one of the glass plate. Second plate was placed over the other one to sandwich sample between plates. A 20g weight was placed on top of upper plate to provide a uniform thin film of sample between the plates. Weight was removed, excess of emulgel sample was scrapped off from edges .The top plate was then subjected to pull by using string to which 50g weight was added. The time required by upper plate to travel a distance of 6cm and separate from lower plate was noted. This was repeated for 3 times. A shorter interval indicates better spreadability.[3]

Spreadablility = M.L/T

M = weight tied to the upper side

L = length of glass slide

T = time in seconds

1.7.5 Extrudability

The developed formulations were filled in collapsible metal tubes and crimped at one end. After removing the cap, tube is pressed to extrude the product from the tube.[3]

1.7.6 Particle size

Particle size of nano-emulsion was measured by using Malvern Nano-zetasizer Zs90. Particle size of nano-emulsion ranges between 10-100nm.

1.7.8 Zeta potential

The magnitude of the zeta potential indicates the degree of electrostatic repulsion between adjacent,similarly charged particle in dispersion, the Zeta potential of the selected formulation was determined by the laser diffraction analysis using particle size analyser.

1.7.9 Drug content determination

Drug content of emulgel was determined by dissolving an accurately weighed quantity of 1g of emulgel in100ml solution of phosphate buffer pH 6.8. 2ml of this solution was diluted to 10ml with buffer solutions. Filter it to obtain clear solution. Determine its absorbance using UV spectrophotometer and analyzed for drug content at 254nm. Drug content was determined from standard curve obtained.

1.7.10 In vitro drug release of Liquorice Extract Emulgel

Diffusion study of emulgel formulations were performed using Franz-diffusion cell. Cellophane membrane was used in Franz-diffusion cell. The cell was locally fabricated and volume of receptor compartment was 20ml. Phosphate buffer of pH 6.8 was used for in- vitro release as receptor medium. The emulgel sample is applied on the membrane and then fixed in between donor and receptor compartment of quality diffusion cell. The receptor compartment contained phosphate bufferpH6.8. The temperature of diffusion medium was thermostatically controlled at 37o ± 0.5oC by surrounding water in jacket and the medium was continuously stirred by magnetic stirrer at speed of 50 rpm. Aliquots, each of 1ml were withdrawn at hourly intervals and replaced by an equal volume of receptor medium for 12hrs. The aliquots were diluted to 10ml with receptor medium and analysed by UV spectrophotometer at 254 nm and %drug release was calculated.[3]

1.7.11 Drug release kinetics

Cumulative drug release study of the optimized formulation, F4 was fitted into models representing zero order, first order, Higuchi's plot and Korsmeyer-peppasplot respectively.

1.7.13 Anti bacterial activity

The anti-bacterial activity of the optimized formulation was determined by agar-plate diffusion method. It was performed by agar-plate diffusion method. The antibacterial activity was performed using E. coli bacteria. Agar nutrient broth was prepared and poured into sterile petri plates and kept aside for drying and cooling. After that E.coli strain were spread by the micron wire loop. A sterile cork borer 6mm diameter was used to drill holes 4mm deep. Then place 0.5gm of gel from each formulation into this holes. Plates were incubated at 27 c for 48hr. Then the zone of inhibition was measured.[7]

1.7.14 Anti-inflammatory activity

The In Vitro anti infammatory activity of liquorice extract was evaluated by albumin denaturation method. Extract was mixed with 1% aqueous solution of fetal bovine albumin. pH ofthe mixture was adjusted using 0.1NHcl. The solution was kept in a incubator at 37ºC for 20 min. Afterwards, denaturation was induced by keeping the reaction mixture at 60±1°C in water bath for 10 min. The mixture was cooled and the turbidity was measured using UV spectrophotometer. Percentage inhibition was calculated using the following equation. For this, a marketed product was considered as a standard and the solution containing no drug was considered as control.[5]

% Inhibition = (Absorbance of control – Absorbance of sample) × 100/Absorbance of controls.

1.7.15 Stability studies

From the prepared liquorice extract nano-emulsion,optimized formulation with highest in-vitro drug release was subjected to stability studies. This studies was carried out at room temperature and humidity conditions as per ICH guidelines and the tests were carried out in a stability chamber. The temperature and humidity conditions used were

- $40^0C \pm 2^0C$ at 75% ₊5%RH
- $25^0C \pm 2^0C$ at 75% ₊5%RH
- $5^0C \pm 3^0C$

Samples were withdrawn at 0 day, 30 day time intervals for a period of 3 months and evaluated for physical appearance, pH, viscosity and drug content.[8]

1.8 RESULTS AND DISCUSSION

1.8.1 Phytochemical tests

Table 2: Phytochemical Tests of Liquorice Extract.

METHODS	PHYTOCHEMICAL GROUP	INFERENCE
Molisch's test	Carbohydrates	Present
Keller-Killiani test	Glycosides	present
Foam test	Saponin glycosides	present
Ferric chloride test	Tannins	Present
Test for flavanoids	Flavanoids	present

Thin layer chromatographic analysis

1.8.2 Thin layer chromatography analysis

Rf value was obtained through TLC analysis by dividing the distance travelled by solute from the distance travelled by solvent. The Rf value was found to be 0.5 cm. The TLC plate showed purple color when seen through UV flurescent light.

Rf = Distance travelled by solute ʎ Distance travelled by solvent

= 3.5/7.0

= 0.5 cm

1.8.3 Determination of UV lambda max

The liquorice extract was scanned by UV spectroscopy and λ max was found to be 254nm.

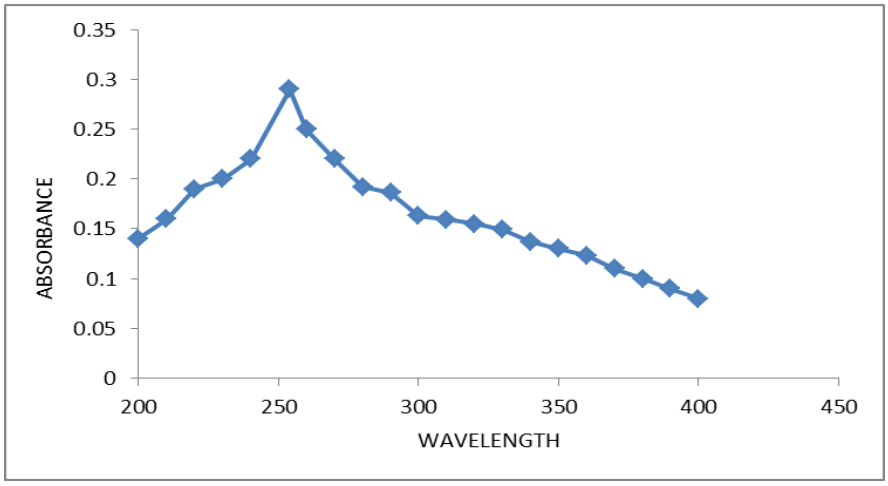
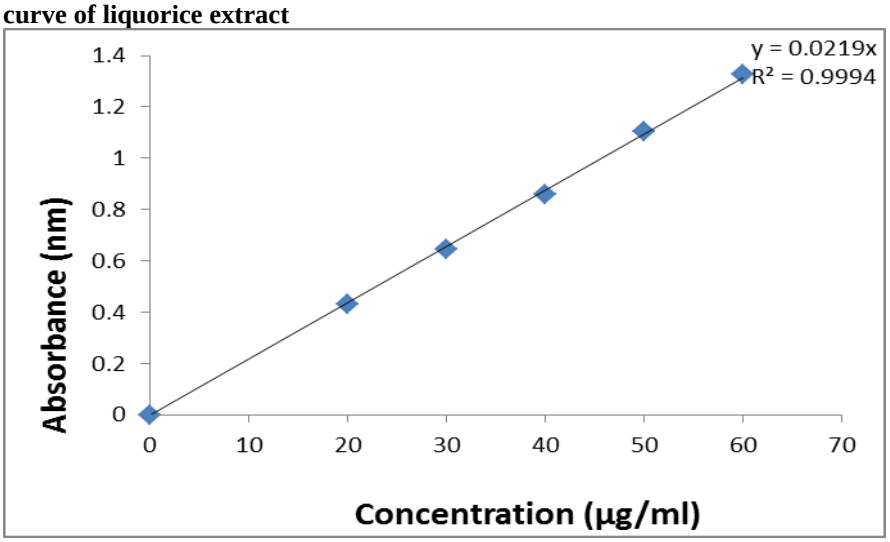


Fig. 4: UV spectrum of liquorice extract in phosphate buffer pH6.8

1.8.4 Calibration curve of liquorice extract



All values are expressed as a mean of ± SD, n=3

Fig .5 Standard calibration curve of liquorice extract in phosphate buffer pH6.8 at 254nm.

The liquorice extract was scanned in UV region (200-400nm) by preparing 1mg/ml solution using phosphate buffer pH6.8 to find out the wavelength of maximum absorption (λ max). The λ max was found to be at 254nm. So the calibration curve of liquorice extract was plotted at this wavelength. Standard calibration curve of liquorice extract was determined in phosphate buffer pH6.8 by plotting absorbance against concentration at 254nm. The calculation of drug content, *in-vitro* release and stability studies are based on this calibration curve.

1.9 Preformulation studies

1.9.1 Solubility profile

Solubility of liquorice extract in various solvent were carried out as shown in table.

Table 2: Solubility of liquorice extract.

NAME OF THE MEDIA	SSATURATION SOLUBILITY OF EXTRACT
Distilled water	Soluble
Ethanol	Soluble
Phosphate buffer pH 5.8	Soluble
Phosphate buffer pH 7.4	Sparingly Soluble

1.9.2 Physical appearance

Liquorice extract is brown coloured powder and smells sweet.

1.9.3 Identification and compatability by FTIR studies

FT-IR studies were conducted in liquorice extract, liquid paraffin, carbopol 940 and tween 80. The FT-IR spectrum is shown below.

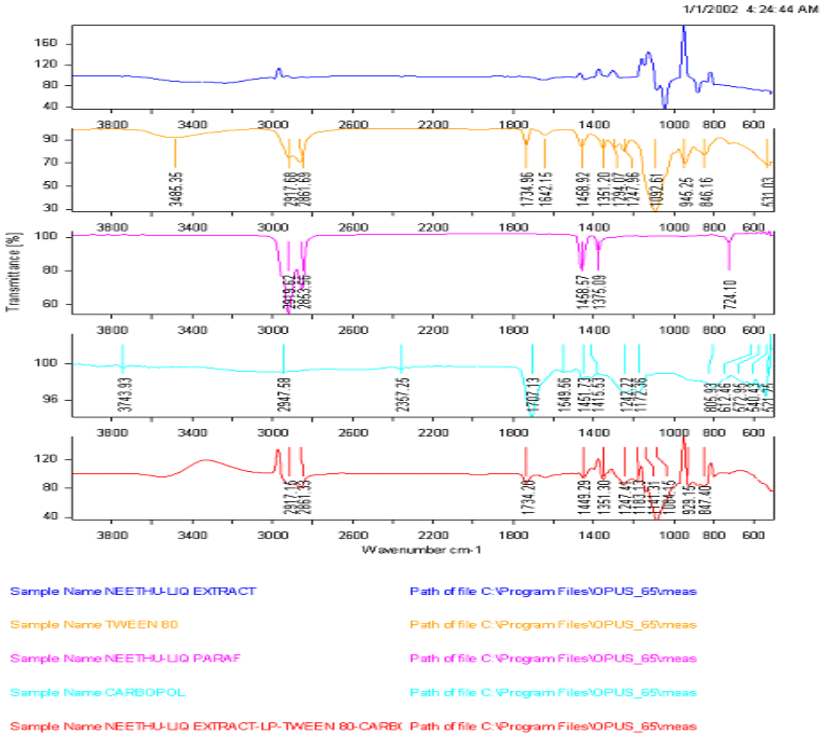


Fig no: 6 FT-IR of liquorice extract, Tween 80, Liquid Paraffin, Carbopol.

During FT-IR, there is no significant change in the peak of the extract in the FT-IR spectrum of of liquorice extract with tween 80,carbopol, and liquid paraffin. It indicates that there is no chemical interaction between the drug and other components of emulgel. This shows that the liquorice extract is compatible with other excipients.

1.10 Evaluation of formulated emulgels

1.10.1 Physical evaluation

Table 3: Physical Evaluation of Formulations.

FORMULATION CODE	COLOUR AND APPEARANCE	HOMOGENEITY	PHASE SEPERATION
F1	YELLOW	HOMOGENOUS	NO
F2	YELLOW	HOMOGENOUS	NO
F3	YELLOW	HOMOGENOUS	NO
F4	YELLOW	HOMOGENOUS	NO
F5	YELLOW	HOMOGENOUS	NO
F6	YELLOW	HOMOGENOUS	NO
F7	YELLOW	HOMOGENOUS	NO
F8	YELLOW	HOMOGENOUS	NO
F9	YELLOW	HOMOGENOUS	NO

The emulgels prepared using carbopol as gelling agent were yellow in colour and it was found to be homogenousand no phase separation was found.

1.10.2 Rheological studies

Rheological studies were conducted on formulations.

Viscosity

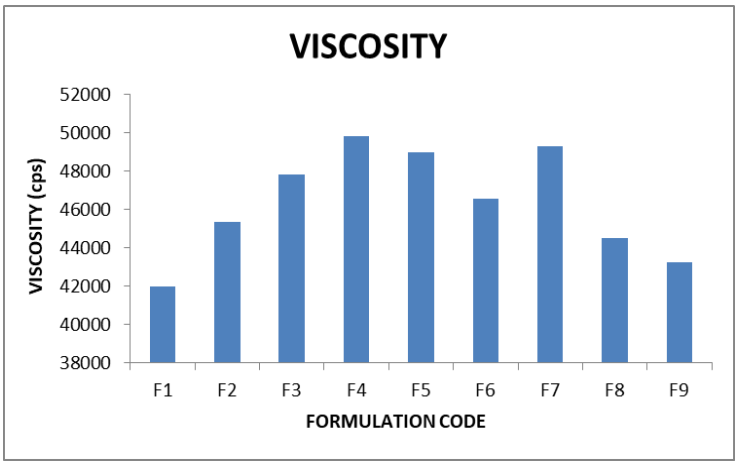


Fig no. 7: viscosity of formulations F1-F9.

The rheological behaviour of all formulated emulgels were studied using Brookfield viscometer at rpm 50 and spindle no.63 was used. The viscosity of the emulgel formulation were found to be in the range in between 4000-5000Cps.

pH determination

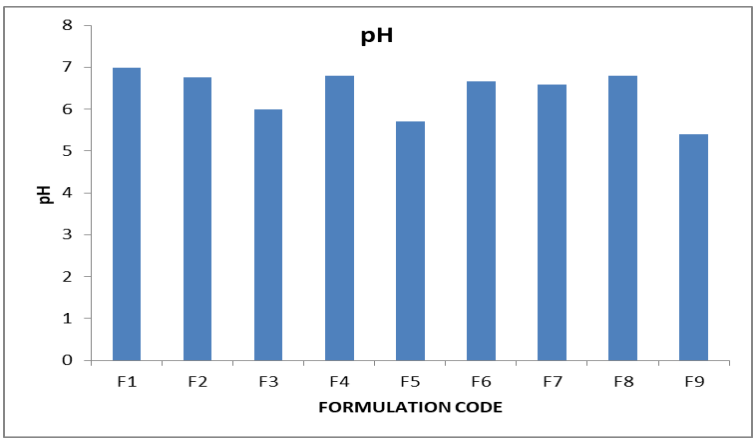


Fig no 8: pH of formulations F1-F9.

The pH values of all the prepared formulation ranged between 5.4-7 which lies within normal pH range of skin and was considered acceptable to avoid any irritation upon application to the skin.

Spreadability studies

The spreadability of formulations were studied using apparatus fabricated in our laboratory.

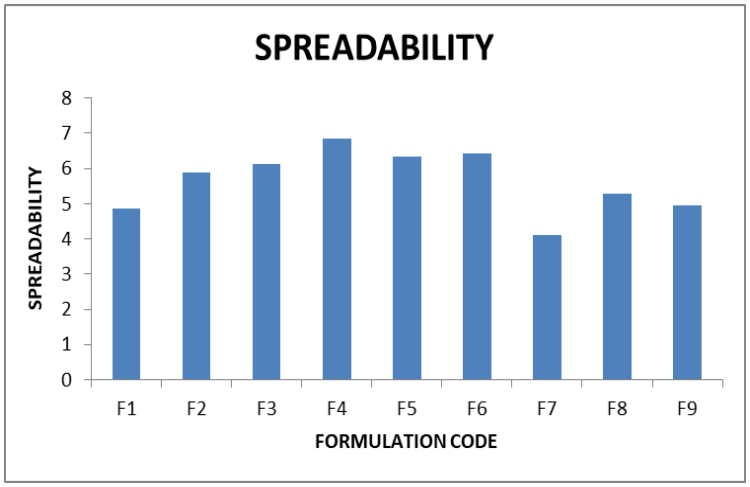


Fig no:9 Spreadability of formulation F1-F9.

Spreadability of formulations were in range of 4.12-6.84g.cm/sec,indicationg good spreadability.

Drug content determination

Drug content of formulated emulgels were determined by UV spectrophotometer at max 254nm and the results of drug content of each formulation is given in the graph below;

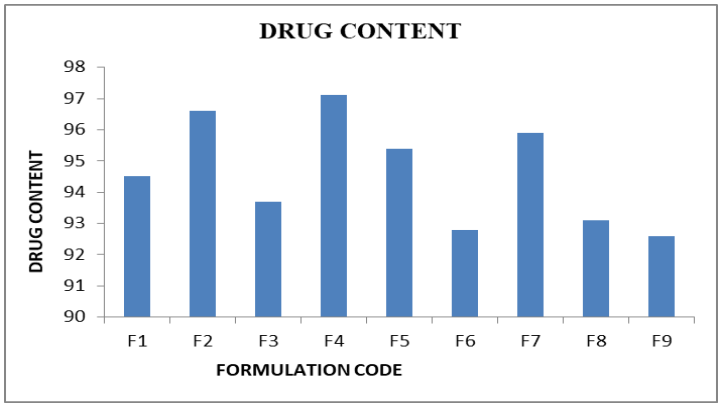


Fig no:10 Drug content of formulation F1-F9

Drug content of formulated emulgels was estimated by UV spectrophotometer at max 254nm and the drug content was calculated from calibration curve. Among all the 9 formulatins, f4 shows the maximum drug content 97.1%.

Particle size and Zeta potential

Table no:4 globule size and Zeta Potential of formulation F1-F9.

Formulation Code	Particle Size (nm)	Zeta Potential(Mv)
F1	120.8	-23.2
F2	96.29	-23.5
F3	77.35	-23.8
F4	73.4	-24
F5	101.3	-24.2
F6	116.3	-24.6
F7	73.38	-23.9
F8	133.6	-22.6
F9	97.19	-24.3

All values are expressed as mean SD,n=3

In-vitro drug release studies:

In vitro drug release of formulations were determined using Franz-diffusion cell fabricated in our laboratory and the results are given below.

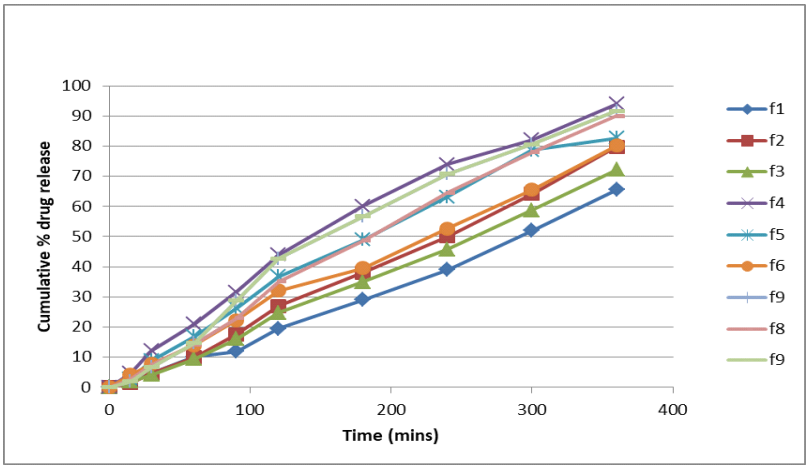


Fig no. 11: cumulative percentage of drug release of formulation F1-F9.

The in-vitro drug release of all the 9 formulations were determined using franz-diffusion cell. Among all the formulations F4 showed greater in-vitro drug release than all other formulation.

Drug release kinetics

The data from in-vitro drug release of the optimized formulation f4 was fitted into various kinetic equation of zero order,first order, higuchi model and korsemeyer peppas model.

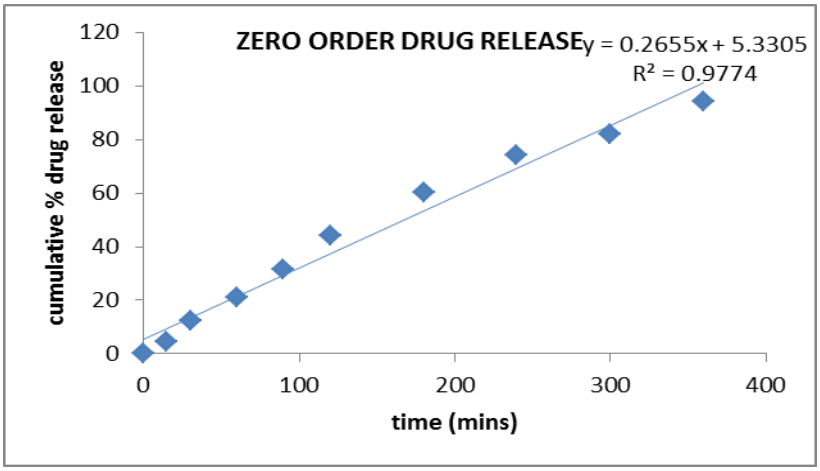


Fig no:12 Zero- order drug release plot of formulation F4.

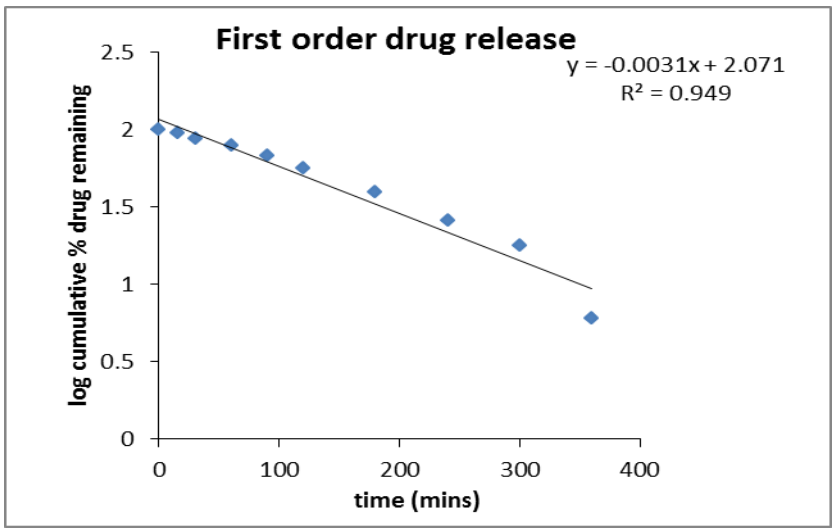


Fig no 13: First-order drug release plot of formulation F4.

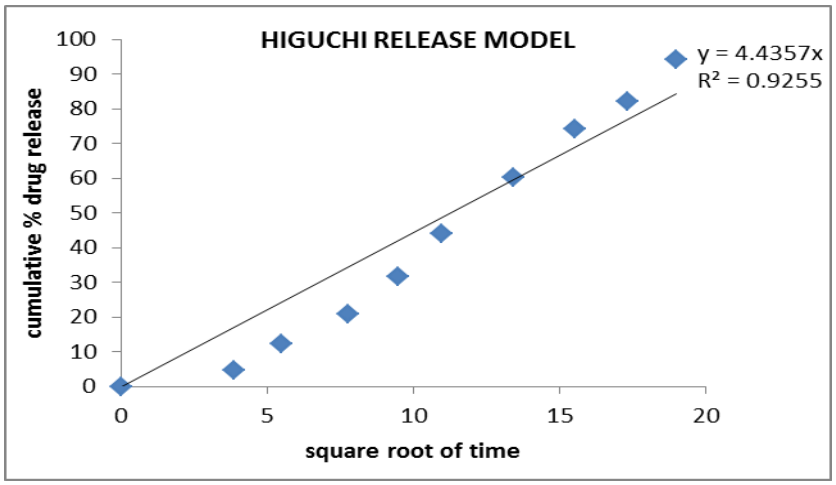


Fig no:14 Higuchi-release model of formulation F4

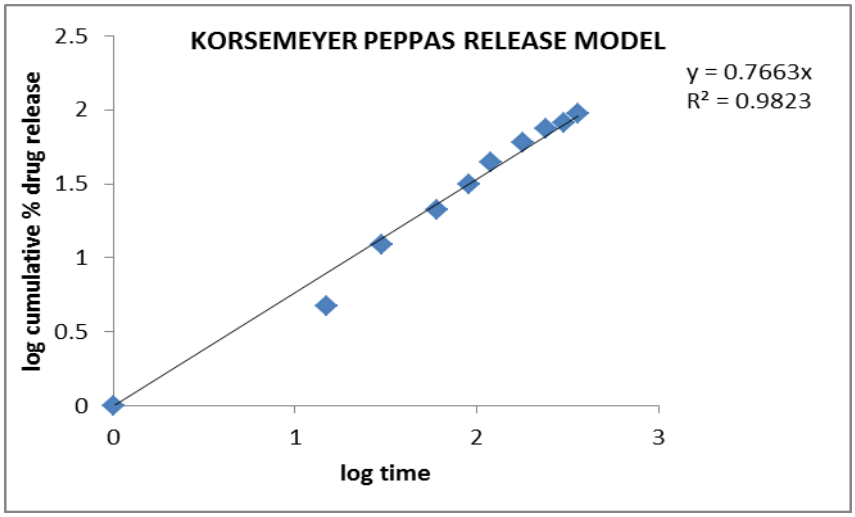


Fig no: 15 Korsemeyer peppas release model of formulation F4.

Table no. 5: Drug release kinetics of optimized formulation F4.

FORMULATION CODE	ZERO ORDER R^2	FIRST ORDER R^2	HIGUCHI R^2	KORSMEYER-PEPPAS R^2
F4	0.9774	0.949	0.9255	0.9823

The value of slope of plot 'n' gives indication of release mechanism.

The 'n' exponent value of best batch was found to be 0.7663. Hence it shows non-fickian release pattern.

Microbial study of optimized formulation

The microbial study was done on the optimized formulation and zone of inhibition was measured.

Table no: 6 Microbial study of optimized formulation.

Formulation code	Zone of inhibition (mm)
F4	19.1mm

Anti – Inflammatory study

Table no. 7: Anti-inflammatory study of optimized formulation F4.

SAMPLE	ABSORBANCE	MEAN ABSORBANCE±SD	INHIBITION (%)
LIQUORICE EXTRACT	0.043	0.043±0.002	29.51%
	0.046		
	0.041		
STANDARD	0.027	0.028±0.03	54.09%
	0.031		
	0.028		
CONTROL	0.06	0.061±0.003	
	0.065		
	0.059		

In vitro anti infammatory studies were carried to relate anti infammatory activity of liquorice extract with standard drug.Percentage inhibition was calculated using the absorbance and it was found that the extract and standard showed 29.51% inhibition and 54.09 %inhibition respectively.

Stability studies of optimized formulation

From in-vitro release studies of prepared formulations of nano-emulsion,F4 showed the best drug release profile. Hence it was used for stability studies.

Table no. 8: Stability studies of optimized formulation F4.

STORAGE CONDITION	SAMPLING INTERVAL	PHYSICAL APPEARANCE		DRUG CONTENT%	IN-VITRO DRUG RELEASE%
		COLOUR	HOMOGEINITY		
40^0c ±2^0c at 75%±5%RH	Initial study	YELLOW	HOMOGENOUS	97.1±0.129	94.8
	30days	YELLOW	HOMOGENOUS	97±0.16	94.7
	90days	YELLOW	HOMOGENOUS	96.9±0.90	94.6
25^0C±2^0c at 60% ±5%RH	Initial study	YELLOW	HOMOGENOUS	97.1±0.129	94.8
	30days	YELLOW	HOMOGENOUS	97.1±0.10	94.8
	90 days	YELLOW	HOMOGENOUS	97±0.58	94.7
5^0C± 3^0C	Initial study	YELLOW	HOMOGENOUS	97.1±0.16	94.8
	30 days	YELLOW	HOMOGENOUS	97.1±0.56	94.8
	90 days	YELLOW	HOMOGENOUS	97.1±0.58	94.8

From the 9 formulations, the optimized formulation F4 was used for stability studies as per ICH Guidelines for 3 months. It showed that the prepared emulgel passed stability studies with no much significant changes in physical appearance, drug content and *in-vitro* drug release.

CONCLUSION

Liquorice extract nano-emulsion was successfully developed using liquid paraffin as oil phase, tween 80 as surfactant, PEG 400 as co-surfactant and water is used as the aqueous phase. The nano-emulsion is formed by phase titration method and phase diagram is used to find the concentration range of nano-emulsion.

From the results obtained it can be concluded that F4 formulation with particle size 73.4nm and drug release with 94% was found to be optimized. From the kinetic studies,it was found that formulation f4 explained by zero-order drug release and korsmeyer peppas plot which indicated non-fickian diffusion and the optimized formulation was found to be stable and have sufficient antimicrobial and anti-inflammatory effect.

As it combines the advantage of an emulsion and gel it can be concluded that extract of liquorice nano-emulgel can be effectively used as a topical dosage form.

ACKNOWLEDGEMENT

It gives me great pleasure to express my deep sense of heartfelt gratitude to the Management,Principle and Faculty members in Crescent College of Pharmaceutical Sciences for all the support in successful completion of the study.

REFERENCE

1. Yadav SK, Mishra MK, Tiwari A, Shukla A. EMULGEL: A NEW APPROACH FOR ENHANCED TOPICAL DRUG DELIVERY. Int J Curr Pharm Res, 2016 Dec 31; 9(1): 15.
2. Varsha S, C AR, Sonam P. PHYTOCHEMICAL SCREENING AND DETERMINATION OF ANTI-BACTERIAL AND ANTI-OXIDANT POTENTIAL OF Glycyrrhiza glabra ROOT EXTRACTS. Vol. 7, J. Environ. Res. Develop. Journal of Environmental Research And Development.
3. Al-Nima A, Qasim Z, Al-Kotaji M. Formulation, evaluation and anti-microbial potential of topical Licorice root extract gel. Iraqi Journal of Pharmacy, 2020 Dec 31; 17(1): 37–56.
4. Kumar Harwansh R, Chandra Patra K, Kumar Pareta S, Singh J, Akhlaquer Rahman M, Harwansh RK, et al. Nanoemulsions as vehicles for transdermal delivery of glycyrrhizin. Vol. 47, Article Brazilian Journal of Pharmaceutical Sciences, 2011.
5. Chauhan S, Gulati N, Nagaich U. Ácido glicirrícico: extracción, cribado y evaluación de la propiedad anti-inflamatoria. Ars Pharmaceutica (Internet), 2018 Jun 20; 59(2).
6. Azadbakht M, Monadi T, Esmaeili Z, Chabra A, Tavakoli N. Formulation and evaluation of licorice shampoo in comparison with commercial shampoo. J Pharm Bioallied Sci, 2018; 10(4): 208.
7. Sing R, Bansal S, Mishra MK. Formulation and Evaluation of Herbal Oral Gel Containing Extracts of Powdered Psidium guajava Linn Leaves with Curcuma longa Linn Rhizomes to Treat Mouth Ulcer. Int J Drug Dev & Res [Internet], 2020; 12(2): 150. Available from: www.imedpub.com
8. ich guidelines - Google Search [Internet]. [cited 2023 Mar 27]. Available from: https://www.google.com/search?q=ich+guidelines&oq=&aqs=chrome.0.35i39i362l8.312548747j0j7&sourceid=chrome&ie=UTF-8