INTERNATIONAL JOURNAL OF DRUG DISCOVERY AND HERBAL RESEARCH (IJDDHR)
10(4): Oct.-Dec.: (2020), 892-899
ISSN: 2231-6078

Research Article

Formulation and Evaluation of Topical dosage drug delivery system for Anti inflammatory activity

Suraj [1] *, Shailendra Singh Chandel [1], Shailesh Gupta [2] and Sandeep Singh [3]
1. Millennium College of Pharmacy, Bhopal, Madhya Pradesh, India
2. Millennium College of Pharmacy and Science, Bhopal, Madhya Pradesh, India.
3. Mission college of Pharmacy, Utter Pradesh, India

Abstract

The main objective of undertaken work was to treat today's major problem that is inflammation which might be caused due to several reasons. To avoid the side effect of synthetic drug there is need to develop a safe and effective herbal formulation. In view of foregoing consideration *Commiphora wightti* herb is highly used by the rural and tribal people in curing various disorders. The aim of the current investigation is evaluation of anti inflammatory activity of *Commiphora wightti* extract . *In-vitro* anti-inflammatory study performed by percentage inhibition of Human red blood cell (HRBC) membrane stabilization method. Four different concentration of extract 1mg/ml, 2 mg/ml, 4 mg/ml and 6 mg/ml were used for each extract. Among which ethanolic extract of *Commiphora wightti* at concentration 6 mg/ml showed 49 % protection of HRBC in hypotonic solution and *A. Commiphora wightti* extract at concentration 6 mg/ml showed 53.89 while combination of extract (1:1 ratio) at concentration 6 mg/ml showed 65.42 % protection of HRBC in hypotonic solution. All the results were compared with standard indomethacin which showed 69.0 % protection at concentration 2.5 mg/ml

Keywords: Natural remedies, anti-inflammatory, Human red blood cell (HRBC) membrane stabilization, hypotonic solution.

Introduction : Ayurveda ancient sciences of life are believed to be prevalent for the last 5000 years in India. It is one of the most noted systems of medicine in the world. Ayurveda is based on the hypothesis that everything in the universe is composed of five basic elements viz. space, air, energy, liquid and solid. They exist in the human body in confined forms like vata(space and air), pitta(energy and liquid) and kapha(liquid and solid). Vata, pitta and kapha together are called tridosha (three pillars of life) .Imbalance in between these will cause pathological condition.[1]

Medicinal plants contain inherent active ingredients to cure disease or relieve pain. The use of traditional medicines and medicinal plant in most developing countries as therapeutic agent for the maintenance of good health has been widely observed.

*** Corresponding Author**

E.mail: shailgpharma@gmail.com

The world health organization estimated that 80% of the population of developing countries relies on traditional medicines, mostly herbal plant drugs for their primary health care. The medicinal property of plant could be based on the anti-oxidant, antimicrobial, antipyretic effect of the phytochemicals present. Traditionally, herbs have been considered to be non-toxic and have been used for treating various problems by the general public and/or traditional medicine doctors worldwide. Although, the literature has documented several toxicity resulted from the use of herbs on many occasions, still the potential toxicity of herbs has not been recognized by the general public or by professional groups of traditional medicine. The use of medicinal plants as raw materials in the production of drug is gaining popularity.[2,3]

Guggul plant commonly known as Commiphora wightii. It is belong to family Burseraceae and Class-magnoliopsida. The use of guggul plant in the treatment of diseases occupies an important place in ayurveda, the traditional medicine system of india. The Atharvaveda one of the four well known holy scriptures (Vedas) of the Hindus, the Atharvaveda is the earliest reference for it medicinel and therapeutic properties . Detained description regarding it action, use and induction as well as the varieties of guggul have been described in numerous Ayurvedic treat including Charaka samhita (1000 BC), Sushruta Samhita (600 BC and Vagbhata seventh century AD). In addition, various medical lexicons were return between twelth and forteen centuries AD. It responsible for reducing fat, indicated for healing Bone Fracture to inflammation, Arthritis, Atherosclerosis, Obesity, Hyperlipidemia, Rheumatism, Haemorrhids, Urinary disorder, skin disease high cholesterol, neuro-degenertion, Parkinson's diseases, mongolism and ageing process. Guggul is a gum resin, historically used for antiseptic and deep penetrating action in the treatment of elevated blood cholesterol and Arthritis. Guggul is effective as weight loss and fat burning agent. It increase white blood cell count and possess strong disinfecting properties.[4-5]

Materials and Methods

Collection of plant material

The stem barks of *Commiphora wightii* were collected from Bhopal. The plant was washed, chopped in to small pieces and dried under shade then powdered coarsely with a mechanical grinder. The powder was passed

through sieve No. 40 and stored in an airtight container for further use.

Preparation of plant powder

The plant was dried under shade and then powdered coarsely with a mechanical grinder. The powder was passed through sieve No. 40 and stored in an airtight container for further use.

Preparation of extracts:

The stem barks of *Commiphora wightii* were collected, washed, chopped in to small pieces and dried under shade then powdered coarsely with a mechanical grinder. The powder was passed through sieve No. 40 and stored in an air tight container for further use. About 100 grams of coarsely powdered plant material was successively extracted by Soxhlet extraction method using solvents with increasing polarity viz. petroleum ether and methanol. Each time before extracting with next solvent, the powdered material was dried in hot air oven. Each extract was then concentrated by distilling off the solvent by evaporation to water bath. All the extracts thus obtained were stored in air-tight bottles at 4ºC for further experiments [5-6]

Preparation of Hydrogel and Hydroalcohalic gel Containing Extract[7-9]:

Hydrogel

Different proportions of Carbopol 934 and Sodium CMC 3:0, 3:1, 2:1, 1:1, 0:3, 1:3 and 1:2 were dispersed in 50 ml of distilled water with continuous stirring. 5 ml of distilled water was taken and required quantity of methyl paraben and propyl paraben were dissolved by heating on water bath and cooled. Propylene glycol 5 % w/v was added and then mixed with first solution. *Commiphora wightii* (1gm) of plant extract was dissolved in minimum organic solution and mixed to the polymer mixture .The volume was made up to 100 ml with distilled water. Finally all the ingredients were then mixed properly with the Carbopol 934 gel with continuous stirring. Triethanolamine was added drop wise to the formulation for adjustment of required skin pH (6.8-7) and to obtain the gel of required consistency (Table 5.1&5.2). The same method was followed for preparation of control sample without adding plant extract. Turbidity and lumping occurred in some batches (F1, F2, F6 and F7) of polymer based gel. Hence, these batches were discarded and remaining batches (F3, F4 and F5) were considered for further studies.

Hydroalcohalic gel

1:2 proportions of Carbopol 934 and Sodium CMC were dispersed in 50 ml of distilled water with continuous stirring. 5 ml of distilled water was taken and required quantity of methyl paraben and propyl paraben were dissolved by heating on water bath. The solution was cooled and then propylene glycol 5 % w/v was added and mixed with first solution. 1.0 gm quantity of each plant extract was dissolved in minimum quantity of ethyl acetate and 30 ml of ethanol added then mixed to the above polymer mixture. The volume was made up to 100 ml with distilled water. Finally all the ingredients were then mixed properly with Carbopol 934 gel with continuous stirring. Triethanolamine was added drop wise to the formulation for adjustment of required skin pH (6.8-7) and to obtain the gel of required consistency (Table 5.1). The same method was followed for preparation of control sample without adding any plant extracts.

Evaluation of Gel Formulation[7-15]:

All prepared formulations of gel were characterized for:

Physical Evaluation

Physical parameters such as color and appearance of the herbal gel were observed manually.

Measurement of pH

The pH of various gel formulations was determined by using digital pH meter. One gram of gel was dissolved in 100 ml distilled water and stored for two hours. The measurement of pH of each formulation was done in triplicate and average value was calculated.

Spreadibility

Spreadibility was determined by the apparatus which consists of a wooden block, provided with pulley at one end. By this method spreadibility was measured on the basis of slip and drag characteristics of gels. An excess of gel (about 2g) under study was placed on the ground slide. The gel was then sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with the hook. A one kg weight was placed on the top of the two slides for 5 minutes to expel air and to provide a uniform film of the gel between the slides. Excess of the gel was scrapped of from the edges. The top plate was then subjected to pull of 80 gms weight with the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5 cm was noted. A shorter interval indicates better spreadibility. Spreadibility was calculated using the formula given below:

$$S = M \times L / T$$

Where, S = Spreadibility, M = Weight in the pan (tied to the upper slide), L = Length moved by the glass slide and T = Time (in sec.) taken to separate the slide completely each other.

Consistency:

The measurement of consistency of the prepared gels was done by dropping a cone attached to a holding rod from a fix distance of 10cm in such way that it should fall on the centre of the glass cup filled with the gel. The penetration by the cone was measured from the surface of the gel to the tip of the cone inside the gel. The distance travelled by the cone was noted after 10sec.

Homogeneity

All the developed gels were tested for homogeneity by visual inspection after setting the gels in the container. They were observed for their appearance and presence of any aggregates.

Viscosity

Viscosity of gel was measured by using Brookfield viscometer with spindle No. 7 at 50 rpm at room temperature. The gels were rotated at 0.3, 0.6 and 1.5 rotations per minute. At each speed, the corresponding dial reading was noted. The viscosity of the gel was obtained by multiplication of the dial reading with factor given in the Brookefield Viscometer manual.

Drug content

1 g of the prepared gel was mixed with 100ml of suitable solvent. Aliquots of different concentration were prepared by suitable dilutions after filtering the stock solution and the drug content was determined measuring the absorbance using UV/Vis spectrophotometer (Shimadzu UV 1700).

Compatibility studies

Fourier transformed infrared (FTIR) spectra technique has been used to study the physical and chemical interaction between herbal extracts and excipients used in formulation by observing any shift in peak of plant extract in the spectrum of physical mixture of plant extract, hydrogel base and ethosomal gel base.

5.5.3 *In-vitro* drug release study of optimized formulation of gel plant extract:

Franz diffusion cell (fabricated in our Lab.) with a diameter 3.7 cm was used in in-vitro release studies. A glass tube with both end open, 10 cm height and 3.7 cm outer diameter was used as a permeation cell. A one gram extract was accurately weighed and placed on a semipermeable cellophane membrane to occupy a circle of 3.7 cm diameter. The loaded membrane was stretched over the lower open end of a glass tube of 3.7 cm diameter and made water tight by rubber band.

Table 1: Formulations of Gel containing Plants extract

Ingredient	F_1	F_2	F_3	F_4	F_5	F_6	F_7	*FH*
Carbopol 934 (gm)	*3*	*3*	*2*	*1*	-	*1*	*1*	*1*
Sodium CMC (gm)	-	*1*	*1*	*1*	*3*	*2*	*3*	*2*
Commiphora wightii (% w/w)	*1*	*1*	*1*	*1*	*1*	*1*	*1*	*1*
Ethanol	-	-	-	-	-	-	-	*30 ml*
Propylene glycol 400 (5%)	*5*	*5*	*5*	*5*	*5*	*5*	*5*	*5*
Methyl Paraben (0.5%) (ml)	0.2ml	0.2 ml	0.2 ml	0.2 ml	0.2 ml	0.2 ml	0.2 ml	0.2 ml
Propyl Paraben (0.2%) (ml)	*5 ml*	*5 ml*	*5 ml*	*5 ml*	*5 ml*	*5 ml*	*5 ml*	*5 ml*
Triethanolamine (ml)	*q.s.*	*q.s.*	*q.s.*	*q.s.*	*q.s.*	*q.s.*	*q.s.*	*q.s.*
Distilled water (ml)	*q.s. to 100ml*	*q.s. to 100ml*	*q.s. to 100ml*	*q.s. to 100ml*	*q.s. to 100ml*	*q.s. to 100ml*	*q.s. to 100ml*	*q.s. to 100ml*

Each formulation contains distilled water up to 100 ml .

Gel containing *Commiphora wightii* plant extract

F_1, to F_7 = Hydrogel , FH = Hydroalcohalic gel

The tube (donor compartment) was immersed in a beaker containing 100 ml of phosphate buffer pH 6.8 (receptor compartment) .The cell was immersed to a depth of 1 cm below the surface of buffer. The system temperature was maintained at 37°±1° and speed was maintained at 30 rpm throughout the experiment by magnetic stirrer (Fig.5.2). Samples 3 ml were withdrawn at intervals of 15, 30, 45, 60, 90, 120 and 180 min, the volume of each sample was replaced by the same volume of fresh buffer to maintain constant volume. Samples were analyzed without dilution or filtration for herbal drug content spectrophotometrically at 206 nm and 359 nm.

Drug release kinetic modeling

The kinetics of hydroalcohalic gel FH release was determined using the release kinetics method of drug release into various kinetic equations: zero order release kinetics, first order release kinetics and Higuchi model.

Accelerated Stability Studies

The optimized formulations were subjected to a stability testing for six months as per ICH norms at a temperature and RH of 40°C ± 2°C/75% RH ± 5% RH respectively. The selected formulations were analyzed for the change in appearance, spreadibility, pH and drug content.[16]

Results and discussion

Extraction

The dried powder of plants were extracted with peteroleum ether and methanol. The solvents were removed by distillation under reduced pressure and the resulting semisolid mass was vacuum dried using rotary flash evaporator to obtain the extract.

During the trial, the excipients concentrations of carbapol and Sodium CMC were gradually increased and then decreased as several problems like homogeneity, spreadibility and viscosity were encountered. These problems occurred in some of the batches (F1, F2, F5 and F7) of polymer based gel containing both extract. Hence, these batches were discarded and remaining batches (F3, F4 and F6) were considered for further study.

The result showed that the developed herbal gel was greenish in color, translucent in appearance and showed good homogeneity with absence of lumps. Formulation F6 had good values of spreadability, viscosity, pH, drug content and during the accelerated stability studies the appearance was clear and no significant variation in spreadability, pH and drug content was observed. Hence Hydroalcohalic gel was formulated from hydrogel F6 formulation and its physiochemical study was found to be good. (Fig.6.1 & Table.6.2)

Percentage drug release of Hydroalcohalic gel FH formulation containing plant Commiphora wightii extract was observed to be 18.31% (at 30 min.) and 69.23% (at 120 min.) respectively. It was observed that addition of ethanol in formulation increase the release by increasing permeation properties of gel. The Hydroalcohoic gel containing extract formulation-FH showed maximum drug release as compared to other formulation. (Table.6.5 Fig.6.2)

Table 6.2: Physical evaluation of all formulations

Batch	*Color*	*Appearance*	*Spreadibility (gm.cm/sec)*	*Consistency (60 mm)*	*Viscosity (cps)*	*Ph*	*Drug content (%)*
F3	*Greenish*	*Homogeneous*	*23.81*	*8*	*16915*	*7.00*	*99.95*
F4	*Greenish*	*Homogeneous*	*24.22*	*8*	*16995*	*7.00*	*99.97*
F6	*Greenish*	*Homogeneous*	*24.34*	*8*	*16924*	*7.00*	*99.95*
FH	*Greenish*	*Homogeneous*	*24.85*	*8*	*16924*	*7.00*	*99.95*

Evaluation of Gel Formulation:

Standard calibration curve of Commiphora wightii plant extract for its active constituent

Standard calibraction curve of *Commiphora wightii* extract was determined by plotting absorbace vs concentraction at 213 nm and it follow the beer's law. The results are shown in Table.6.4 and Fig.6.3

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

Percentage drug release of Hydroalcohalic gel FH formulation containing plant Commiphora wightii extract was observed to be 18.31% (at 30 min.) and 69.23% (at 120 min.) respectively. It was observed that addition of ethanol in formulation increase the release by increasing permeation properties of gel. The Hydroalcohoic gel containing extract formulation-FH showed maximum drug release as compared to other formulation. (Table.6.5 Fig.6.2)

S.No	Concentration (µg/ml)	Absorbance
1.	Blank	0.000
2.	0.2	0.059
3.	0.4	0.141
4.	0.6	0.212
5.	0.8	0.283
6.	1.0	0.341

Table 6.4: Standard calibration curve of Commiphora wightii

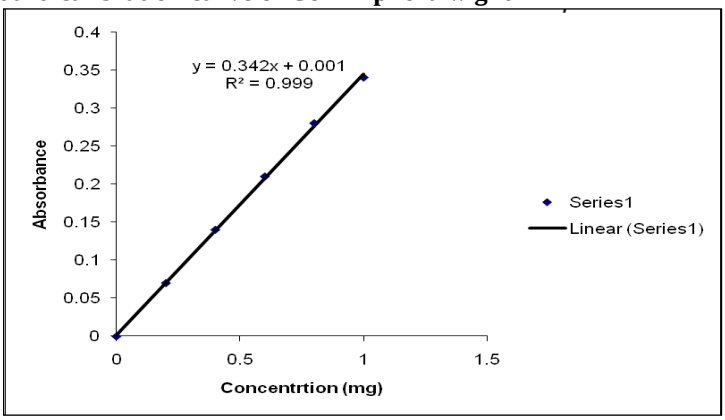

Figure 6.3: Standard calibration curve of Commiphora wightii at 213 nm

Stability Study

The formulated gels were subjected to stability studies. No color fading was observed for all prepared gels. The pH of all formulations remained unchanged and was found to be within the range of 6.2-7.2. The viscosity and spreadability of all gels remained unaltered and found to be within the range. The drug content was found to be in the limit 90% -103% for all gel formulation. (Table.6.14)

Table 6.5: Percentage Drug release of Optimized Formulation Gel at 213 nm

Time Interval (Min)	% Drug release of Formulation	
	F6	FH
15	8.31	12.23
30	14.56	18.31
45	20.91	27.56
60	28.38	35.91
90	39.23	51.38
120	51.15	69.23

FH= Hydroalcoholic gel containing Commiphora wightii plant extract , F_5= Hydrogel

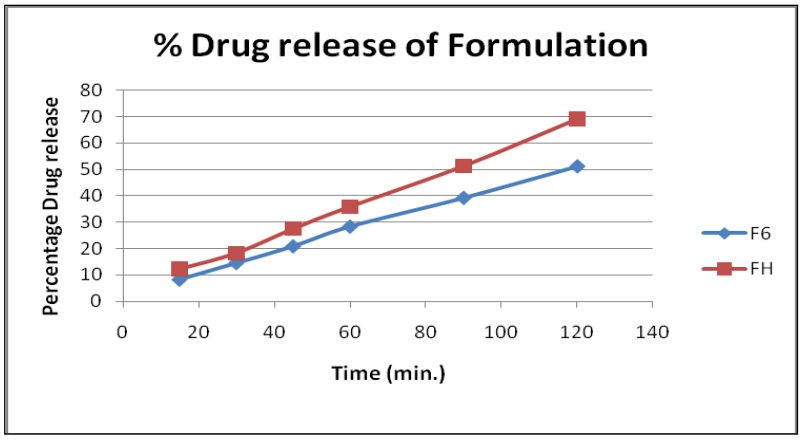

Figure 6.4: Release profile of Hydrogel F-6, Hydroalcohalic gel FH

Table 6.14: Accelerated Stability study of formulated gel

Batch	*Color*	*Appearance*	*Spreadibility (gm.cm/sec)*	*Consistency (60 Sec)*	*Viscosity (cps)*	*Ph*	*Drug content (%)*
F₆	*Greenish*	*Homogeneous*	*19.53*	*5*	*22230*	*6.98*	*99.77*
FH	*Greenish*	*Homogeneous*	*22.13*	*8*	*16951*	*7.01*	*99.86*

(F_6= Hydrogel , FH=Hydroalcohalic gel)

Conclusion

Natural remedies are more acceptable in the belief that they are safer with fewer side effects than the synthetic ones. Herbal formulations have growing demand in the world market. In the undertaken study an attempt has been made to establish that herbal gel containing *Commiphora wightii* extract that can be used as an alternative remedy for management and treatment of inflammation related disorder and disease

Reference

1. Kokate C.K., Purohit A.P. and Gokhale S.B. (2005). *A Text-book of Pharmacognosy*, 31st edition, Nirali Prakashan
2. Sharma Alok (2008). Herbal medicine for market potential in India: An Overview. *Academic Journal of Plant Sciences*, IDOSI Publications, 1(2): 26-36.
3. *Bozzuto Anne (2000). Homeopathy, Herbs and Hypnosis Common Practices, In Complementary and Alternative Medicine, Jacksonville Medicine.*
4. Prasad R S & Sukh Dev ,: Chemistry of Ayurvedic crude drugs IV, (guggulu resin Commiphora mukul):absolute chemistry of mukulol, Tetrahedron, 1976, 32, 1437.
5. Formica J. V., Regelson W.: Review of the biology of quercetin and related bioflavonoids, Fd Chem. Toxic., 1995, 33(12) ,1061-1080.
6. Kokate C.K., Purohit A.P. and Gokhale S.B. (2005). *A Text-book of Pharmacognosy*, 31st edition, Nirali Prakashan, 37, 48-52, 57.
7. A Gupta *et al.*, Formulation and evaluation of topical gel of diclofenac sodium using different polymers, Drug Invention Today 2010, 2(5),250-253
8. Das K, Dang R, Machale UM, Fatepuri S, Formulation and evaluation of herbal gel containing stevia leaves extract, The Pharma Review, 2010, 8(44), 112-118.
9. Prakash RP, Rao R. NG, Soujanya C, Formulation, evaluation and anti-inflammatory activity of topical etoricoxib gel, Asian J. pharmaceutical and clinical research, 2010, 3(2), 126-129.
10. P. Anitha et. al, Ethosomes - A noninvasive vesicular carrier for transdermal drug delivery, Anitha *et al.*, Int. J. Rev. Life. Sci., 1(1), 2011, 17-24
11. K Pavan Kumar *et al*, Ethosomes-A Priority in Transdermal Drug Delivery, International Journal of Advances in Pharmaceutical Sciences,1 (2010) 111-121
12. Jain S, Tiwary AK, Sapra B, Jain NK.,Formulation and Evaluation of Ethosomes for Transdermal Delivery of Lamivudine, *AAPS PharmSciTech*. 2007, 8(4): Article 11
13. A. K. Barupal *et al*, Preparation and Characterization of Ethosomes for Topical delivery of Aceclofenac, Indian J Pharm Sci. 2010 Sep-Oct; 72(5): 582–586.
14. Das K, Dang R, Machale UM, Fatepuri S, Formulation and evaluation of herbal gel containing stevia leaves extract, The Pharma Review, 2010, 8(44), 112-118.
15. Kumar L, Verma R, In vitro evaluation of topical gel prepared using natural polymer, Int. J Drug Delivery, 2010, 2, 58-63
16. ICH Topic Q 1 A (R2) Stability Testing of new Drug Substances and Products, Note for guidance on stability testing: stability testing of new drug substances and products (CPMP/ICH/2736/99), European Medicines Agency, August, 2003.