ISSN: 2287-6898
International
Journal of Bio-Pharma Research
Volume 8, Issue 8 (2019) pp. 2763-2768
Research Article
Open Access

Formulation and evaluation of *Boswellia serrata* resin gel by using different gelling agents

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Abstract: The main objective of the present research work was to develop herbal gel of *Boswellia serrata* (Shallaki gum) for Antiarthritic activity to achieve greater therapeutic effect. Rheumatoid arthritis is a chronic, metabolic disorder which affects joints and periarticular tissue. The plant *Shallaki* is the best traditional medicine for the treatment of rheumatoid arthritis. The motive of this work is to formulate an effective formulation for the treatment of rheumatoid arthritis without any side effect as seen in synthetic drugs because the use of synthetic NSAID'S creates problem-related to the gastrointestinal tract which may further complicate the situation. Hence there is a need to use in Herbal formulation, *Shallaki* is very effective in osteoarthritis, juvenile in rheumatoid arthritis, soft tissue fibrolite, and spondylitis without any side effect. The *Boswellia serrata* (Shallaki) resin gel by using a different gelling agent like Carbopol, HPMC K4M, and Pluronic F127 gives a better therapeutic result. All the formulations (F1 to F8) were subjected for evaluations like physical appearance; pH was found to be 6.09%, in-vitro drug release study was found to be 90.66% at 8 hrs, viscosity was found to be 66800cp, spreadability was found to be 22.12gm\sec. FTIR results showed no interaction between drug and polymers. *Boswellia serrata* is one specific Ayurvedic remedy that was proceeded to extract the gum resin for the treatment of rheumatoid arthritis. The benefits of Boswellia are relatively well explained the focus mostly to reduce the inflammation or pain caused due to rheumatoid arthritis. Formulation (F5) shows the best result of drug release 90.66% at 8 hrs which containing 0.2% Carbopol and 4% Pluronic F127 as a gelling agent.

Key words: *Boswellia serrata*; *Shallaki*; Gelling agents; Traditional; Rheumatoid arthritis; Herbal gel.

Introduction

The oleo-gum resin of *Boswellia serrata* Family Burseraraceae, a tree commonly found in india is used for its patent Antiarthritic and anti-inflammatory activity[1] and has beenmentioned in the ancient ayurvedic text i.e. Sushruta Samhita[2] and *Charaksamhita* the gum contains triterpenic acid β-boswellic acid[3] as the principle constituent which is responsible for its anti-inflammatory activity[4].

Currently there is a greater global interests in non synthetic natural drug derived from plant herbal sources due to better tolerance and decreased adverse drug reaction[5]. However, there is a lack of supporting studies regarding the formulation and evaluation aspect. A document on quality control for medicinal plant material by the *WHO* [6] And the note for guidance on specifications, by the committee for proprietary medicinal product (CPMP) [7] are positive measured in this direction thus the present study was carried out to formulate gel of *Boswellia serrata* extract using different gelling agent in varying and to evaluate its physical parameters and to set up specifications for the finished medicinal product.

The resin is obtained by making scrapes in the trunk of the various *Boswellia species (Burseraceae*), and collecting the dried resin gums from the trees later.[8,9] Good quality resin is produced only for 3 years, after which the quality of the collected resin decreases significantly; therefore, the tree should be left to rest for some years after the harvesting period.[10] *B. serrata* has poor oral bioavailability with an elimination half-life of 4.5±0.55 h. Thus topical delivery of *B. serrata* is the preferred alternative to oral dosage form. But topical delivery is difficult due to its high lipophilicity (log P 8) [11]

Topical gels formulation gives a proper drug delivery system at desired concentration of drug because these are less oily and can be simply remove from the skin. Gel formulations have good applications property and reliability in the

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comparison to cream, emulsion, semi-solid and ointments. Gel formulations are typically transparent or translucent, water based semisolid with good spreading properties and aesthetic characteristic containing a high ratio of solvent that shows no steady-state flow.Topical drug delivery system is most convenient method for the delivery of drug via mucus membrane or skin because it can easily reach to organ or targeted tissue of human body to achieve better therapeutic effect.

Drug *Boswellia serrata*

Scientific Name: *Boswellia serrata*
Family: *Burseraceae*
Common Name: *Shallaki, Kunduru*
Ayurvedic Name: *Shallaki gum*

Figure 1: *Boswellia serrata*

Chemical Composition:

Boswellia serrata is reported to contain 60-85% resins (mixtures of terpenes), 6-30% gums (mixture of polysaccharides), and 5-9% essential oil. Resin portion is composed of pentacyclic triterpenes, in which Boswellic acid is the active functional group. Gum portion consists of pentose and hexose sugars with some oxidizing and digestive enzymes. The essential oil is a mixture of monoterpenes, diterpenes, and sesquiterpenes.

Materials and Methods

Boswellia serrata powder was received from Sunpure Developers Pvt. Ltd., Mumbai., Carbopol940, Pluronic F127, HPMC K4M, Triethanolamine, Ethanol, propyl paraben, Methyl paraben, and Rosemerry oil etc.

Preparation of gel:

Preparation of gel with Carbopol 940*:*

1. Preparation of gel containing *Shallaki extract* & gelling agent of Carbopol 940 soak in water for 2hr.
2. Neutralized with Triethanolamine with continues stirring.
3. Weights of drug dissolve in preweighed propylene glycol with ethanol.
4. Transfer 3 into 1 & agitate for 20min.
5. This dispersion allows hydrating& swell for 60 min adjust p^H with the desired p^H range is (6.8 to 7.0).
6. During ph adjustment mixture stirred gently with spatula to form homogeneous gel.

Preparation of gel with HPMC K4M:

1. Accurately Weighed 1gm of drug was placed to a beaker and dissolve in 1ml of propylene Glycol into which preservative was added.
2. HPMC K4 M was made to disperse in distilled water then heated up to 70-900°C with continually stirred and it was allowed to cool.
3. Then 1%w\v drug loaded to propylene glycol solution was added to HPMC K4 M preparation.
4. Stirred strongly to mix in cold condition & water was added to make up the volume up to 20ml and stirred in mechanical stirred well and got uniformed gels.

Preparation of gel with Pluronic F127:

1. Pluronic F127solution were prepared by dissolving the weighed amount of Pluronic F127 in water and kept in a refrigerator overnight.
2. Gel formulation is prepared by dissolving Methyl paraben & propyl paraben in hot water.
3. Neutralized with Triethanolamine with continues stirring.
4. Weights of drug dissolve in preweighed propylene glycol with ethanol.
5. Transfer the all ingredient Methyl paraben & propyl paraben, propylene glycol, Ethanol, Rosemerry oil.
6. During ph adjustment mixture stirred gently with spatula to form homogeneous gel.

Table 1: Composition of various *Boswellia serrata* Resin Gel formulations

S.No.	Ingredients (gm)	F1	F2	F3	F4	F5	F7	F8	F6
1.	*Shallaki*	1	1	1	1	1	1	1	1
2.	Carbopol	0.1	0.2	0.3	-	0.2	0.3	0.5	0.5
3.	HPMC K4M	-	-	-	0.5	-	-	0.5	0.5
4.	Pluronic F127	-	-	-	-	4	4	4	4
5.	Methyl paraben	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06
6.	Propyl paraben	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06
7.	Glycerin	1	1	1	1	1	1	1	1
8.	Ethanol	5	5	5	5	5	5	5	5
9.	Rosemmery oil	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
10.	Triethanolamine	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

11.	Propylene glycol	1	1	1	1	1	1	1	1
12	Dist.Water (upto)	20	20	20	20	20	20	20	20

Evaluation of prepared topical Gel

Physical Evaluation:

Physical parameters such as colour and appearance were evaluated as shown in table no 3**.**

Homogeneity:

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container for their appearance and presence of any aggregatesas shown in table no 3**.**

pH:

The pH of various gel formulations were determined by using digital pH meter. 2.5gm of gel was accurately weighed and dispersed in 25ml of distilled water and stored for two hours. The measurement of pH of each Formulation was carried out in triplicate and the average values are represented. The pH of dispersions was measured using pH meteras shown in table no 3**.**

Spreadability:

Spreadability was determined by the apparatus which consists of a wooden block, which was provided by a pulley at one end. By this method Spreadability was measured on the basis of slip and drag characteristics of gels. An excess of gel (about 2 g) under study was placed on this 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. Weight of 1 kg was placed on the top of the slide for 5 minutes to expel air and to provide a uniform film of the gel between the slides. Excess of the gel was scrapped off from the edges. The top plate was then subjected to pull of 50 g. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 6.5 cm be noted. A shorter interval indicates better Spreadabilityas shown in table no 3**.** Spreadability was calculated using the following formula:

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

Where, S = Spreadability, 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.

Viscosity:

Viscosity of herbal gel was determined by using Brookfield rotational viscometer at 6rpm. Each reading was taken after equilibrium of the sample at the end of two minutes. The viscosity determination of samples was repeated three timesas shown in table no 3**.**

Stability Study:

The stability study conducts by ICH guideline. It showed No significance change in properties of the optimized formulation & the drug release. Short term stability studies were performed in a Stability chamber over a period of 3 month on the promising *Boswellia serrata* gel. Sufficient quantity of gel formulation were packed in stability container and kept in a Stability chamber at Temperature 45^0c &RH 75%. Samples were taken for the PHandviscosity, were performed to determine the stability profileas shown in table no 3**.**

Results and Discussion

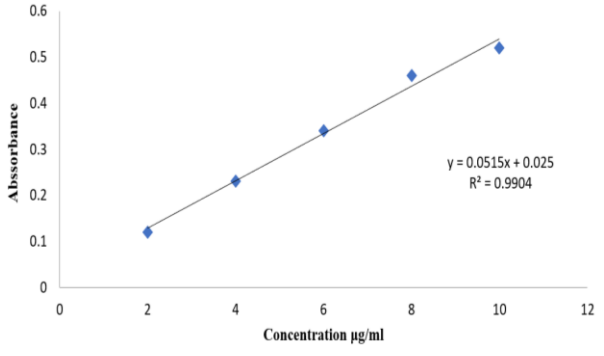
50 mg of *Boswellia serrata* resin was weighed accurately and dissolved in 50 ml phosphate buffer pH 5.5, the solution marked as stock solution-1 from this solution 10 ml of solution was withdrawn in 100 ml volumetric flask and make the volume up to 100 ml by distilled water. Then solution was sonicated for 10 min. This solution marked as stock solution-2.

- From stock – 2, dilution having concentration 2 µg/ml, 4 µg/ml, 6 µg/ml, 8 µg/ml, and 10 µg/ml was prepared by distilled water.
- Above prepared solution were observed in double beam UV- spectrophotometer to measure the absorbance in increasing order of concentration.

Table 2: Calibration curve of *Boswellia serrata* resin in phosphate buffer

Sr. no.	Concentration (ug/ml)	Absorbance (λ_{max} observed at 254nm)
1	2	0.1200
2	4	0.2300
3	6	0.3400
4	8	0.4600
5	10	0.5200

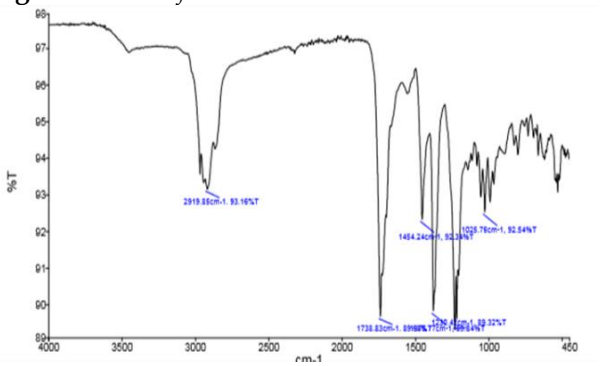
Figure 2: Calibration Curve of *Boswellia serrata (Shallaki) Extract*



Drug excipient compatibility study
The drug and excipient were taken in 1:1 ratio and mixed properly using a poly bag. Now the mixtures were transferred into the glass vials and samples were placed in stability chamber at 400C for 21 days. Glass vials filled with plane drug and polymers were also placed in the same way.

Through Fourier Transform Infrared Spectroscopy: Drug excipient compatibility study was confirmed by FTIR analysis.

Figure 3: *FTIR of Boswellia serrata*



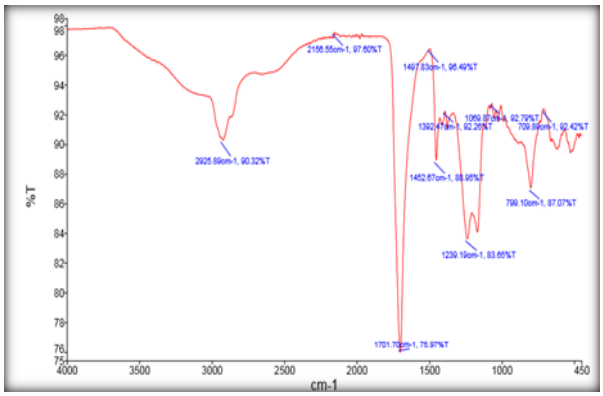


Figure 4: *FTIR of Boswellia serrata* + Carbopol 940

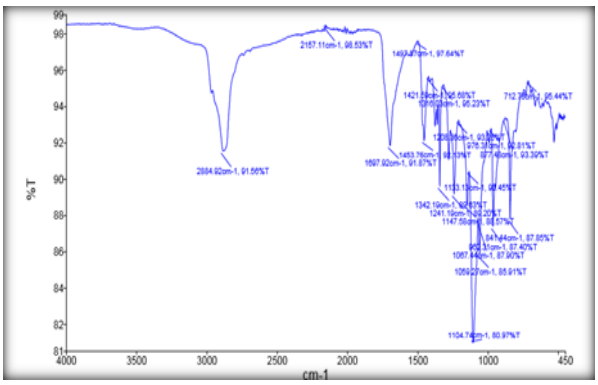


Figure 5: *FTIR* of *Boswellia serrata* + Pluronic F127

Table 3: Physical Appearances, PH, Viscosity, Spreadability andHomogeneityof Various Formulation.

Sr.no	Batch	Appearance	Homogeneity	PH	Spreadability(gm\sec)	Viscosity
1	F1	yellow	Homogeneous	6.08	21.29	64500
2	F2	yellow	Homogeneous	6.08	15.21	41000
3	F3	yellow	Homogeneous	6.08	18.20	75330
4	F4	yellow	Homogeneous	6.08	13.08	58000
5	F5	yellow	Homogeneous	6.09	20.12	66800
6	F6	yellow	Homogeneous	6.08	21.13	33000
7	F7	yellow	Homogeneous	6.08	22.06	32666.6
8	F8	yellow	Homogeneous	6.08	12.06	70500

Evaluation Studies
Physical Appearances, PH, Viscosity, Spreadability and Homogeneity of Various Formulations.

***In-vitro* drug release study:**
The *in-vitro* diffusion studies were carried out using Franz diffusion cell apparatus and semi-permeable cellophane membrane. Cellophane membrane, previously soaked overnight in phosphate buffer 5.5 was mounted by tied and sandwiching between the donor and receiver compartment. Franz diffusion cell 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 sample was accurately weighed and placed on a semi permeable 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. The tube (donor compartment) was immersed in a beaker containing 100 ml of phosphate buffer pH 5.5 (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 Samples 5 ml were withdrawn at intervals of 0, 1, 2, 3, 4 and 5 hour, the volume of each sample was replaced by the same volume of fresh buffer to maintain constant volume. The samples were filtered through Whatman filter paper, diluted up to 10 ml and absorbance was taken by UV spectrophotometer at respective ʎmax 254. The experiment was carried out triplicate and average value is reported.

Table 4: *In-vitro* diffusion study of *Boswellia serrata* [F1-F8]

Time (min/hr)	% Drug release							
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
1	42.6	43.2	42.4	44.5	48.5	40.2	39.2	30.0
2	50.1	50.4	51.2	51.6	52.3	50.5	51.6	52.1
3	70.3	70.8	71.6	72.5	77.1	73.2	74.5	76.5
4	81.2	82.5	82.31	82.21	87.2	80.8	81.9	82.6
5	83.1	83.21	84.54	86.1	90.66	87.1	88.6	89.5

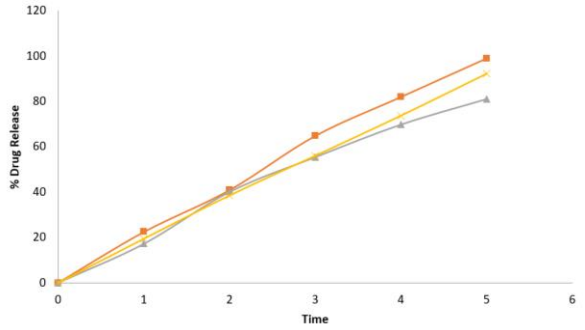


Figure 5: % cumulative release of differentformulation in phosphate buffer (pH 5.5).

Stability Study:
Sufficient quantity of gel formulation were packed in stability container and kept in a Stability chamber at Temperature 45^{0}c & RH 75%.

Table 5: Stability study of formulation

Sr.no	Parameter	Stability after 1 month of a optimized batch F5	Stability after 2 months of a optimized batch F5	Stability after 3 months of a optimized batch F5
1	Colour	yellow	yellow	yellow
2	Physical Appearance	No change	No change	No change
3	Drug Content (%)	98.54%	98.50%	98%
4	PH	6.09%	6.09%	6.09%
5	Consistency	Smooth	Smooth	Smooth

Conclusion

In our analysis, we are here with concluding that development of *Boswellia serrata* (Shallaki) gel is suitable topical drug delivery method to ease drug application, minimize extensive phase1 metabolism, thereby help to improve bioavailability and also minimize side effects. Different formulations of *Boswellia serrata* (Shallaki) extract, evaluation parameters results were observed, F5 formulation was found to be the best formulation.

Shallaki extract formulation of FTIR studies concluded that there was no interaction between drug and excipient. (Carbopol, Pluronic F127, methyl paraben, Propyl paraben, propylene Glycol, Rosemerry oil.). Carbopol, HPMC K4M, Pluronic F127 (20%) used as Gelling agent. Combination of Carbopol and Pluronic shows better gelation phenomenon. While HPMC fails to formulate desired gel consistency.

The FTIR studies revealed that, the formulated product is a mixture of drug and the polymers used, but not the reaction product with the excipient used. A good In vitro drug release was observed for formulation F5.

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Cite this article as:

Gaware Rutuja J., Gaikwad V. M., Nagoba Shivappa N., Hindole S. S. Formulation and evaluation of *Boswellia serrata* resin gel by using different gelling agents. *International Journal of Bio-Pharma Research*, Volume 8, Issue 8 (2019) pp.2763-2768.

http://dx.doi.org/10.21746/ijbpr.2019.8.8.3

Source of support: Nil; **Conflict of interest:** Nil.