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Formulation and Evaluation of Boswellia Serrata Nanogel

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ABSTRACT
This study has been done as an attempt to formulate Boswellia serrata in the form of nanogel which can be expected to reduce the dose frequency and increase the drug loading capacity. The main objective of this study is to develop a nanogel with reduced particle size in order to reduce dose dependence side effect, to increase the drug bioavailability, decrease drug toxicity and to produce desired transdermal drug delivery. The present study involves formulation of Boswellia serrata nanogel by solvent emulsification method by incorporating it into the gelling agent Carbopol 940, methyl paraben, EDTA and PEG 400.The formulated nanogel was evaluated for particle size, zeta potential, viscosity, spreadability, pH, invitro drug release studies and drug release kinetic studies.
Keywords: Transdermal drug delivery, nanogel, Boswellia serrata.

I. INTRODUCTION

Nanotechnology is the science and technology of small things in particular things that are less than 100nm in size.

Nanogels-based nanoplatforms have become a tremendously promising system of drug delivery .Nanogels are constructed by chemical crosslinking or physical self- assembly exhibit the ability to encapsulate hydrophilic or hydrophobic ,including but not limited to small molecule compounds and proteins, DNA/RNA sequences, and even ultra small nanoparticles within their 3D polymer network.

The term nanogels are defined as nanosized particles formed by physically or chemically crosslinked polymer network that swells in a good solvent. Nanogel has controlled and sustained drug release at target site, improving the therapeutic efficacy and reducing the side effects. Drug loading is relatively high and may be achieved without chemical reaction this is an important factor for preserving the drug activity.

Nanogels a type of systemic drug delivery carrier are hydrogels with a three dimensional tunable porous structure and particles size in submicrometer range from

20 to 250nm. Nanogels are composed various natural polymers, synthetic polymers or combinations of both which contribute to encapsulation of small molecules, oligonucleotides, and even proteins. These unique properties equip nanogels with the abilities to enable drug delivery, diagnostics and imaging

Nanogel based drug delivery system is highly biocompatible and biodegradable due to this characteristics it is highly promising field now a days.

The most beneficial feature of nanogels is their rapid swelling and deswelling properties and higher drug loading capacity.

Nanogels typically range from 20-200nm in diameter and hence are effective in avoiding the rapid renal exclusion but are small enough to avoid the uptake by the reticuloendothelial system. Good permeation capabilities due to the extreme small size. More specifically, it can cross the blood brain barrier (BBB)

Nanogel based formulations confirm to be useful scaffold in nanomedicine including biosensors, artificial muscles, biomaterials, biochemical separation, cell culture systems, biocatalysis, photonics, biomimetics, drug delivery, anticancer therapy. However nanogels were explored from a longer period of time in relation with trends for synthetic procedures not only for drug delivery systems but others like quantum dots, MRI contrast agents and other diagnostic agents.

II. MATERIALS AND METHODS

Drug name: BOSWELLIA SERRATA
Phytoconstituent: Boswellic acid Family: Burseraceae
Mechanism of action: Boswellic acids exhibit potent antiinflammatory properties in vitro and in vivo. Triterpenes in boswellic acid reduce the synthesis of leukotrienes in intact neutrophils by inhibiting 5- LOX, the key enzyme involved in the

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biosynthesis of leukotrienes, which mediate inflammation

Extraction:

Extraction of boswellic acid from Boswellia serrata was performed by maceration process. The resin of Boswellia serrata was finely powdered and placed in a container filled with menstrum (ethanol and water (50:50)) and was left to stand for three days with occasional stirring. The material was then compressed and pressed to obtain the extract the resulting extract and was subjected to filtration to obtain crude product of Boswellic acid.

Formulation of Boswellia serrata nanogel:

Accurately weighed quantity of boswellic acid (200mg) was dissolved in 10ml of organic phase which comprises of ethanol and triethanolamine (10:0.3). This organic phase is bath sonicated for about 15 minutes for dissolving the surfactant. Temperature of this phase is maintained at 700C.

The aqueous phase was prepared by dissolving weighed quantity of Carbopol940, PEG4000 and methyl

paraben in sufficient quantity of water. Temperature of this phase is also maintained at 700C. Accurately 10ml of this aqueous phase was added to the organic phase at 700C and mixture was sonicated for 5 minutes by probe sonicator. The mixture was gradually cooled to room temperature to induce formation of gel.

III. 3. RESEARCH ENVISAGED

3.1Particle size and zeta potential:

Properties like particle size and zeta potential were determined by Malvern particle size analyzer.

3.2Determination of pH:

Measured by using pH meter.

3.3Viscosity determination:

Determined using brookfield viscometer. 0.5g of sample without dilution is taken and using spindle number 63 viscosity is determined at different rpm at 25oC.

3.4Spreadability coefficient:

It consists of a wooden block which is attached to a pulley at one end. Spreading coefficient is measured on the basis of „slip. and „drag. characteristics of nanogel. A ground glass slide is fixed on the wooden block. An excess of nanogel under study was placed on the glass slide. The Nanogel formulation was sandwitched between the two slides having the same dimensions that of fixed ground slide. The weight of 100 grams was placed on the top of the two slides for few seconds to provide uniform film of nanogel between the two slides. A measured quantity of weight was placed in the pan attached to pulley with the help of hook. The time (in seconds) required by the top slide to cover a distance of 7 cm was noted. A shorter interval indicates better spreading coefficients

3.5 Invitro release study of Boswellia serrata nanogel:

Nanogel preparation was taken in a dialysis membrane of 5cm of length and suitably suspended in beaker containing 200ml of diffusion medium (phosphate buffer saline pH 7.4). The medium was maintained at temperature of 37-37.5oC. It was stirred by means of magnetic stirrer at a constant speed. Sample of 1ml (diffusion medium) was withdrawn every one hour for 24 hours and replaced the diffusion medium. So that the volume of diffusion medium was maintained constant at 200ml. The sample was measured spectrophotometrically at 259nm.

3.6 Drug release kinetics:

Zero order kinetics:

The diffusion model of Boswellia serrata nanogel follows zero order kinetics. The graph is plotted on as Time Vs Cumulative percentage drug release.

Higuchi plot:

The graph is plotted on as Square root of time Vs Cumulative percentage drug release.

IV. RESULTS AND DISCUSSION

4.1 Particle size and zeta potential:

The particle size of Boswellia serrata nanogel shows the size range of about 638.5nm. The smaller particle size enhances the sustained release of drug.

Zeta potential of the formulation was found to be -27.4 which confirms the particle size of the formulation remains stable and prevents the particle from formation of aggregates.

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Figure -1

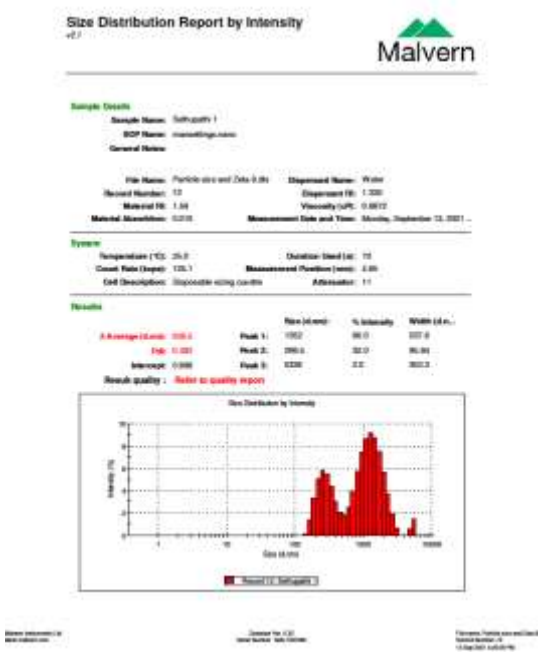
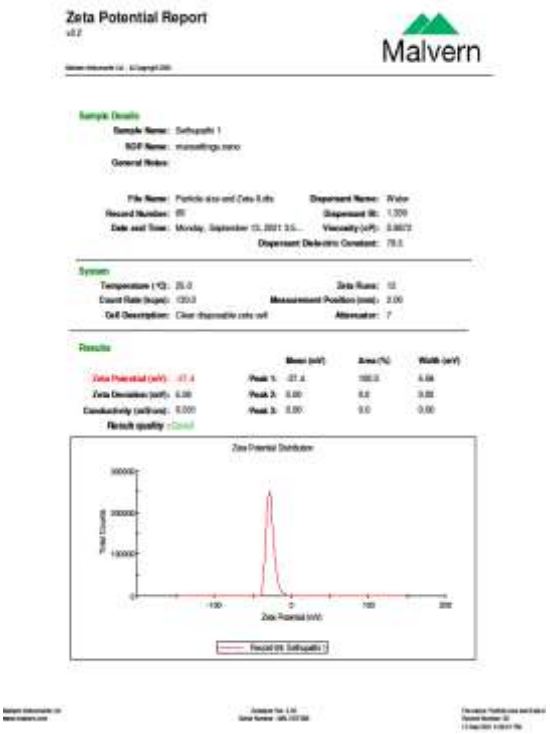


Figure -2



4.2 Determination of pH:

The pH values of all the prepared formulations were ranged between 5.9 to 6.5 is considerable to avoid skin irritation on application on the skin.

4.3 Viscosity studies:

The measurement of viscosity of prepared nanogel was done using Brookfield viscometer.

The formulation BSNF5 shows better viscosity of 26.5 m-1 kg s-1 as compared to other formulations.

Table 1

FORMULATION CODE	VISCOSITY (m^{-1} $kg\ s^{-1}$)
BSNF1	27.3
BSNF2	29.4
BSNF3	28.7
BSNF4	27.3
BSNF5	26.5

4.4 Spreadability coefficient:

The spreadability of various concentration of Carbopol 940 is 28.1gm.cm/s. All the formulation shows better spreadability.

Table 2

FORMULATION CODE	SPREADABILITY COEFFICIENT (gm.cm/s.)
BSNF1	27.3
BSNF2	25.4
BSNF3	28.7
BSNF4	27.3
BSNF5	28.1

4.5 Comparitive Invitro drug dissolution studies:

The In vitro drug release of profiles of all Boswellia serrata nanogel formulation are represented in the table 3 .

The In vitro drug release depends upon the Carbopol 940 concentration. The In vitro release of

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boswellic acid from nanogel varies. In formulations BSNF1, BSNF2, BSNF3 drug release was because of high carbopol940 concentration, where the amounts of drug release after 24 hours from formulation BSNF4, BSNF5 were found to be 90% and 97% respectively, due to the optimization of concentration of carbopol940 with constant PEG4000 concentration throughout the formulation.

The BSNF5 shows sustained release up to 24 hours by releasing the drug concentration of 97.46%.

Table 3

S.NO	TIME	BSNF1	BSNF2	BSNF3	BSNF4	BSNF5
1	0	0	0	0	0	0
2	2	5.614	6.817	7.268	7.51	9.025
3	4	11.041	13.651	14.554	15.05	17.065
4	6	16.468	20.485	21.790	22.59	25.105
5	8	21.895	27.319	29.126	30.13	33.145
6	10	27.322	34.153	36.363	37.66	41.185
7	12	32.749	40.987	43.699	45.2	49.225
8	14	38.176	47.821	50.935	52.74	57.265
9	16	42.633	55.055	58.271	60.28	65.305
10	18	49.030	61.891	65.502	67.8	73.345
11	20	54.457	68.725	72.844	75.3	81.385
12	22	59.884	75.559	80.08	82.8	89.425
13	24	65.311	82.393	87.416	90.43	97.465

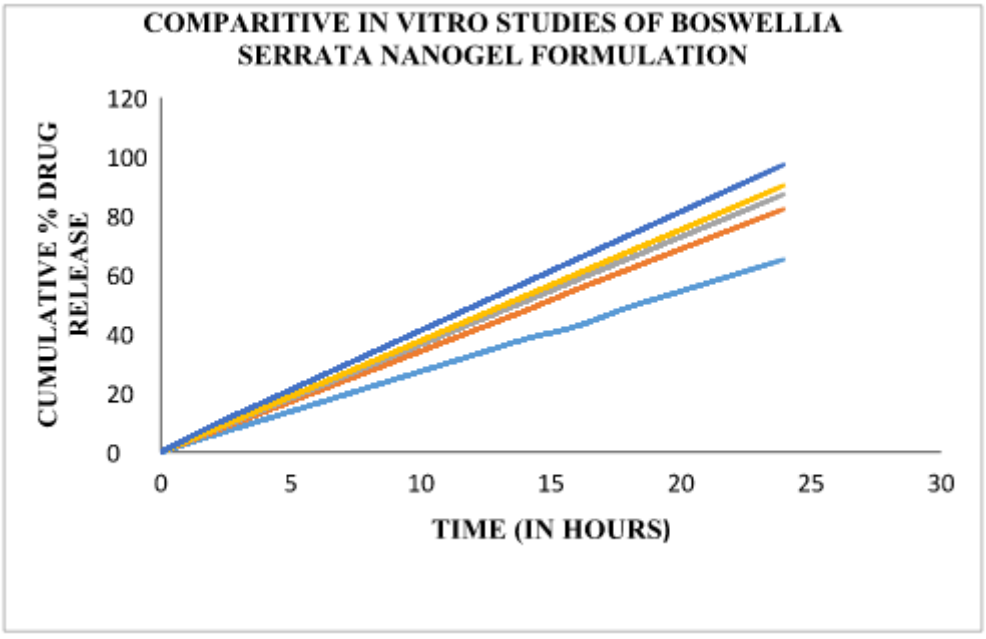

Figure -3

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4.6 Drug release kinetic studies:

Table -5

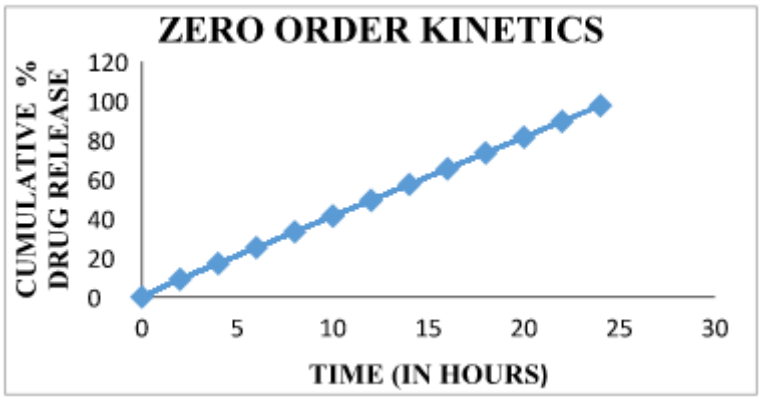

Table -6

Table -7

ZERO ORDER KINETICS	HIGUCHI PLOT
r^2	r^2
0.99	0.93

From the above drug release kinetics it was found that it follows diffusion mediated release and zero order release pattern.

V. SUMMARY AND CONCLUSION

In the study, we have taken effort to prepare nanogel of Boswellia serrata, the gel formed is quite stable.

The particle size and zeta potential of the optimized formulation BSNF5 was found to be 638.5nm and -27.4 respectively.

The pH, viscosity and spreadability of optimized formulation shows better results.

The Invitro drug release of formulation BSNF5 was found to be 97.46% and it is selected as optimized formulation.

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Drug release kinetic study shows, it follows zero order kinetics. Hence, we can anticipate that, the Boswellia serrata nanogel will be prioritized in future pharmaceutical developments.

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