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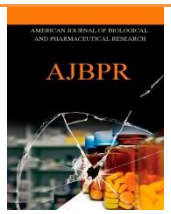

DESIGN AND *INVITRO* EVALUATION OF NANOGEL CONTAINING *MENTHA PIPERITA*

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ABSTRACT

The aim of this work is to design a *Mentha piperata* essential oil loaded nanogel for analgesic effect and to evaluate the drug content and *invitro* drug release studies. Nanogels based materials have high drug loading capacity, biocompatibility, and biodegradability which are the key points to design a drug delivery system effectively. The pursuit of this research article is to concisely describe the recent development of nanogel drug delivery system in terms of drug loading and swelling of drug from nanogels. Nanogel is prepared by modified emulsification-diffusion method by using swelling polymer like carbopol 940.The formulated gel was evaluated for particle size Zeta potential, Drug content, Entrapment efficiency, *In vitro* drug diffusion studies, *In vitro* skin permeation studies.

INTRODUCTION

Nanogels may be defined as nano-sized hydrogel systems which are highly cross linked systems in nature involving polymer systems which are either co-polymerised or monomers. Sudden outbreak in the field of nanotechnology have introduced the need for developing nanogel systems which proven their potential to deliver drugs in controlled, sustained and targetable manner. With the emerging field of polymer sciences it has now become inevitable to prepare smart nano-systems which can prove effective for treatment as well as clinical trials progress [1,2].

Traditionally in the name of gels we have heard of semisolid formulations with three dimensional networks of organic systems encompassing fluids and drugs. Majorly these systems have been the part of traditional system of topical drug delivery for local effects. Prospects of targeted drug delivery perhaps could not been established with these preparations. The significance of nano-sized microgel and hydrogel has arisen due to specific delivery system anticipation. Wide variety of polymer systems and the easy alteration of their physico-chemical characteristics have given advantage for versatile form of nanogel formulations. Recent studies at clinical level have shown promising value of nanogels. Nanogels have revolutionized the field of gene therapy, since delivery of gene has now become possible within cellular organelles for gene silencing therapy systems. Nanogels are typical formulations mainly of the size range of 100 nm, by varying solvent quality and branching the volume fraction can be altered variably to maintain a three dimensional structure. The overall review suggests that innovation in this field shall bring forth sound support to cancer therapy in future [3, 4].

Peppermint is extracted from *Mentha piperata* ,is widely used in food, cosmetics and medicines. It has been proven helpful in symptomatic relief of the common cold. It may also decrease symptoms of irritable bowel syndrome and decrease digestive symptoms such as dyspepsia and nausea, although more research is needed. It is used topically as an analgesic and to treat headaches [5].

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MATERIALS AND METHODS

Mentha piperata (ACE) was gift sample obtained from commercial market. The chemicals used for the following research are Spectrum grade. Carbopol 940 was purchased from Loba Chemie Pvt. Ltd. Mumbai.

Methods of Preparation

Preparation of Mentha piperata loaded Nanodispersion:

The Nanodispersion of the Mentha piperata was prepared by modified emulsification-diffusion method 100 mg of Mentha piperata was weighed and dissolved in 10 ml ethylacetate containing polymer. This organic phase containing drug polymer mixture was added into the 30ml of aqueous phase containing Tween 80, with constant stirring at 5,000-10,000 rpm using High speed homogenizer. Addition of organic phase was done with the help of syringe positioned with needle directly into the aqueous stabilizer solution at the rate of 0.5 ml/min. The resulting dispersion was stirred for 6 min at 10,000-25,000 rpm and was subjected to the sonication for 5- 10 min. Then double distilled water was added slowly to the dispersion with subsequent stirring for1 hour to induce diffusion of organic solvent into the continuous phase and leading to the formation of nanodispersion. Gels of the Nanodispersion were prepared by dispersing a gel forming agent carbopol 940 in the Nanodispersion of Mentha piperata by using high speed stirrer. The pH was adjusted to the 7.0 by using triethanolamine to form the gel and Mentha piperata enriched gels were stored at room temperature [4-8].

Extraction process:

The coarse powder of whole plant of *Mentha piperatta* was extracted with methanol in herb: menstrum ratio of 2:4 by hot solvent extraction by heating with it for 12 hr. The methanolic extract was concentrated under reduced pressure to obtain a greenish yellow coloured crude extract substance contains essential oil respective for analgesic effect.

Evaluation of Nanogel:

Measurement of particle size of the formulation

The mean size and polydispersity index of the size distribution of the selected nanogels were determined by using Malvern Mastersizer 2000 MS (Malvern Instruments UK). The mean particle size and size distribution were recorded.[7]

Determination of Zeta potential

The zeta potential of the selected formulation was measured by Beckman coulter (Beckman Coulter DelsaTM NanoCommon) [7, 8].

Total drug content

A 0.5 gm of the prepared nanogel was diluted with 10 ml of ethyl acetate and filtered with a 0.45 µm filter. Total drug content was determined by UV spectrophotometry at 254nm using the formula [7, 8].

$$TDC = \frac{\text{Total amount of Nanogel} \times \text{Amount of drug in 0.5 gm Nanogel}}{\text{Amount of nanogel in gm W Initial drug} - \text{W Free drug}}$$

***In vitro* drug diffusion studies:** Dialysis membrane diffusion technique was used to study in-vitro diffusion of drug from the prepared nanogel formulations. The receptor medium used was freshly prepared phosphate buffer pH 7.5. Dialysis membrane (Molecular weight cut off- > 12, 000, Hi media) previously soaked overnight in the receptor medium was on the Franz's Diffusion cell assembly. 0.5 g of formulation was placed in the donor compartment and the assembly was kept on the multi station diffusion study apparatus (make Orchid Scientific) at 37^0 C ± 2^0C and stirred at 700 RPM. Aliquots of 0.5 ml were withdrawn at pre-determined time intervals (0.5, 1, 2, 3, 4, 5, 6, 8, and 24 hrs) and immediately replaced by same volume of the fresh medium. The aliquots were suitably diluted with the dissolution medium and analyzed by UV-Vis Spectrophotometer at 254 nm (λmax of crud extract in methanol). The data obtained from the *In vitro* diffusion studies were fitted to various kinetic equations to find out the mechanism of *Mentha piperata* release from the nanogels [9-17].

RESULTS AND DISCUSSION

Physical characterization

The formulation shows a clear nanogel with good consistency, transparency, flow property and spreadability. It shows a uniform distribution particle and uniform dispersion with the polymer.

Evaluation of Nanogel:

Scanning electron microscopy (SEM)

Shape and surface morphology of the Nanogel prepared with optimized parameters was observed by scanning electron microscopy. The study shows that most of the Nanogel particles were moderately spherical in shape, the surface of the particle showed a characteristic smoothness, and the particle size was in the nanometric range, as depicted by SEM. Some of the particles were found to be in clusters and mostly the overall formulation shows uniform dispersion of extract all over the gel as shown in the Figure 1.

Average particle size, PDI and Zeta potential

The particle size analysis revealed that, the Nanogel was in the nanometer range. The size of the nanoparticles was affected by the homogenization time and the concentration of carbopol 940. The size of the Nanogel containing *Mentha piperata* was found to be between 224.8nm to 557.6 nm which were tabulated below. The stability of the formulated Nanogel was evaluated by

measuring the zeta potential of the Nanogel (it shown between the desired range ±30 mV).Zeta potential of *Mentha piperata* loaded formulations was in the range of -21.04 to -33.40 mV and Polydispersity index was found to be between 0.840 to 0.866.

Drug content

The prepared formulations were analyzed for drug content. It was observed that the drug content in the prepared Nanogel was satisfactory and the drug was uniformly distributed in all the formulations. The percentage drug content is highest for F5 formulation was about 88.92 %.

***Invitro* drug diffusion studies:**

The mean (n = 3) cumulative amounts of drug diffuse through the egg membrane were performed for 12 hours, analyzed and their values are shown in Table 2. Among this five formulation F5 shows better release pattern as desired i.e., 69.90±3.64 for 12 hrs, due to good homogenization time, polymer concentration and uniform dispersibility of crude extract in the nanogel.

Table 1. Formulations of nanogel containing Mentha Piperata extract

Sl. No	Mentha Piperata extract	Carbopol 940	Ethylacetate	Tween 80	Distilled water	Homogenization time
F1	100 mg	10 mg	10 ml	0.5 %	10 ml	1000 RPM
F2	100 mg	20 mg	10 ml	1.0 %	10 ml	2000 RPM
F3	100 mg	30 mg	10 ml	1.5 %	10 ml	3000 RPM
F4	100 mg	40 mg	10 ml	2.0 %	10 ml	4000 RPM
F5	100 mg	50 mg	10 ml	2.5 %	10 ml	5000 RPM

Table 2. *Invitro* drug diffusion studies for formulation F1-F5

Time in hrs	F1	F2	F3	F4	F5
1	7.25±0.05	6.43±0.05	5.60 ±0.10	9.10± 1.42	8.56±1.66
2	12.36±1.24	12.90±1.24	10.54±2.20	19.32±2.44	16.73±2.64
4	18.45±2.20	18.99±2.20	15.39±2.40	30.96±3.42	28.89±3.66
6	28.62±2.02	24.51±2.02	23.14±3.24	41.76±3.98	39.58±3.32
8	34.79±2.10	29.32±2.10	32.69±2.62	52.11±3.44	51.82±3.44
12	52.33±3.20	47.32±3.20	51.66±3.14	71.79±3.22	69.90±3.64

Figure 1. SEM- Surface Morphology of Nanogel

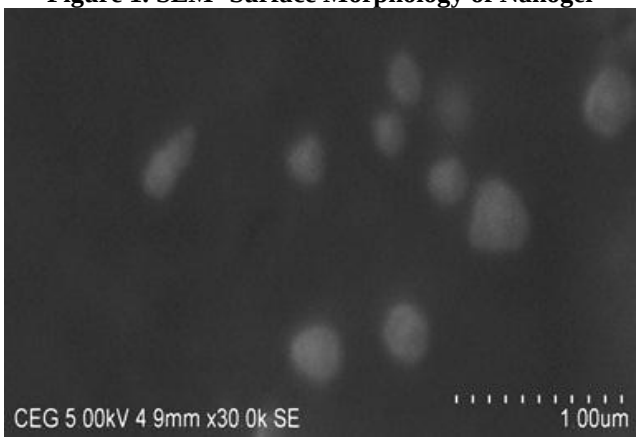
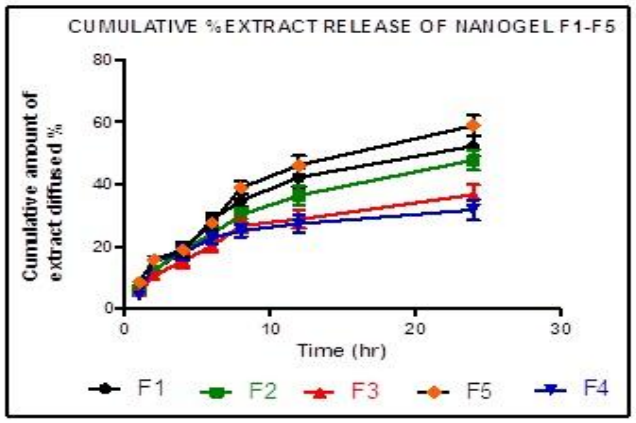


Figure 2. Cumulative % drug diffused from Nanogel



CONCLUSION

Nanogel containing *Mentha piperata* was prepared and evaluates by Modification emulsification method followed by Homogenization. From the results it can be concluded that F5 is the best formulation among all the formulation. So Modification emulsification method, Carbopol 940 and 5000 RPM Homogenization time are desired and optimized selected parameters for the formulation of Nanogel.

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