



PREPARATION AND EVALUATION OF MICROEMULSION CONTAINING CLOVE OIL AND PEPPERMINT OIL AS ACTIVE COMPOUND

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ABSTRACT

Microemulsion are one of the potential and emerging drug carrier systems that helps to improve drug release and enhance the bioavailability of poorly aqueous soluble drugs. This study was designed to formulate and evaluate microemulsion containing clove oil and peppermint oil. Microemulsion was prepared using tween 80 as a surfactant and ethanol as a co - surfactant. The microemulsion formulation characterized for its particle size, viscosity, conductivity, pH, zeta potential and stability. The mean droplet size of clove oil and peppermint oil microemulsion was found in the range of 11-96nm and 11-68nm. The viscosity of the prepared microemulsions were found to be low. In the stability study there are no phase separation occur after centrifuged at 3000 RPM for 30 min and even after stored for 30 days.

Keywords- Clove oil, Microemulsion, Novel drug delivery system, Peppermint oil.

INTRODUCTION

Microemulsions are novel drug delivery system which are thermodynamically stable, clear isotropic mixture of oil, surfactant and co-surfactant. Microemulsion plays an important role in improving the solubility as well as the bioavailability of poorly soluble drug. The microemulsion can enhance the oral bioavailability due to its capacity to increase the permeability and solubility of the drug in the GIT. It also improves the delivery of the drug through dermal transport because of its better permeation rate^{1,2}.

Microemulsions are thermodynamically stable mixtures of oil, water and surfactant. The stability is due to the presence of large quantities of surfactants. Microemulsion are mainly 3 types:²

Oil in water type microemulsion

In this type oil droplets are dispersed in a continuous aqueous phase.

Water in oil type microemulsion

In this type water droplets are dispersed in a continuous oil phase.

Bi-continuous microemulsion

In this type micro domain of oil and water are inter dispersed within the system.

Clove oil (CO) and Peppermint Oil (PO) are essential oil extracted from *Syzygium aromaticum* and *Mentha x piperita* respectively. They are already reported for antimicrobial, antifungal and anti-inflammatory activity^{3,4}. Clove oil and peppermint oil are volatile in nature and highly affected by heat, thus incorporating them in a microemulsion system can increase the self-life of the oils.

MATERIALS AND METHODS

All the chemicals and reagents obtained and used are of analytical grade. Clove oil and peppermint oil and tween 80 were obtained from Himedia Lab Pvt. Ltd. Ethanol was obtained from Changshu yangyuan Chemical, China.

Preparation of microemulsion

The oil in water microemulsion formulations were prepared by phase titration method⁵. A series of microemulsion formulations were prepared using clove oil and peppermint oil as oil phase, Tween 80 as a surfactant, ethanol as co-surfactant and deionized water as aqueous phase. A mixture (S_{mix}) of surfactant and co-surfactant was prepared by taking 3:1 ratio respectively. Oil and S_{mix} of different weight ratios of 1:9, 2:8, 3:7, 4:6, 5:5, 6:4, 7:3, 8:2, and 9:1 were taken for both the oils. These mixtures were mixed for 2 hours on magnetic stirrers, and then titrated with deionized water in a drop-wise manner and mixed thoroughly by magnetic stirrer. The titration of water was stopped until the turbid mixtures changed into a clear solution. The amounts of water added in each group were recorded and noted. The samples were stored for 48 h for observation after that prepared microemulsion was subjected to further analysis.

Initially 9 different formulations of each oil were prepared as per composition shown in the Table 1. Transparency of the formulation mixtures were observed visually after 48 hours. Only transparent formulations were further analyzed.

EVALUATIONS

Visual observation

Visual observation of the prepared was done to check the Parameters such as transparency, phase separation etc. The formulations having better clarity and with no phase separation were selected for further analysis.

Measurement of pH

The pH of the prepared microemulsion formulations were determined by using a calibrated digital pH meter.

Electrical Conductivity

The electrical conductivity of the formulations was determined by Nano partica SZ 100. Initially, the conductivity meter is calibrated with distilled water and then, the conductivity of the formulations was measured. The electric conductivity was calculated in mS/cm.

Viscosity

The viscosity of the prepared microemulsions were measured by using Nano Partica SZ 100.

Particle size analysis

The particle size or the globule size of selected formulations was analyzed using Nano partica SZ 100. Particle size analysis was performed by DLS (Dynamic light scattering). The sample is

taken in a cuvette and placed in the particle size analyzer and its particle size was measured.

Emulsion stability test

Change in droplet size over the period of 24 hours, 7 days and 28 days were analyzed to determine kinetic stability of the microemulsion^{6,7}.

The microemulsion were centrifuged at 3000 RPM (Eppendorf Centrifuge 5430 R) for half an hour.

Zeta potential analysis

The surface charge of the microemulsions are measured by the SZ-100 by measuring the zeta potential of a solution. The sample is injected into a cuvette and placed in the particle size analyzer and the zeta potential of the prepared microemulsion were measured. The zeta potential is mostly used to check of dispersion stability of a sample⁸.

Table 1: Initial formulations with different oil and S_{MIX} ratio

Sl no	Formulation code	Oil: S _{mix}	Transparency
1	PF1	9:1	Turbid
2	PF2	8:2	Turbid
3	PF3	7:3	Turbid
4	PF4	6:4	Turbid
5	PF5	5:5	Turbid
6	PF6	4:6	Turbid
7	PF7	3:7	Transparent
8	PF8	2:8	Transparent
9	PF9	1:9	Transparent
10	CF1	9:1	Turbid
11	CF2	8:2	Turbid
12	CF3	7:3	Turbid
13	CF4	6:4	Turbid
14	CF5	5:5	Turbid
15	CF6	4:6	Transparent
16	CF7	3:7	Transparent
17	CF8	2:8	Transparent
18	CF9	1:9	Transparent

Table 2: Final formulations selected for the further evaluation

Sl no	Formulation Code	Transparency
1	CF7	Transparent
2	CF8	Transparent
3	CF9	Transparent
4	PF6	Transparent
5	PF7	Transparent
6	PF8	Transparent
7	PF9	Transparent

Table 3: P_H, viscosity and conductivity of the selected formulations

Sl No	Formulation code	pH	Viscosity (mPa.s)	Conductivity (mS/cm)
1	PF6	5.9	0.893	0.131
2	PF7	5.8	0.896	0.131
3	PF8	6.3	0.895	0.154
4	PF9	6.2	0.897	0.134
5	CF7	7.1	0.898	0.139
6	CF8	7.2	0.896	0.139
7	CF9	6.9	0.896	0.154

Table 4: Stability of the prepared formulations at 24hr, 7 days and 28 days

Sl no	Formulation code	24 hours	7 days	28 days
1	CF7	Stable	Stable	Unstable
2	CF8	Stable	Stable	Stable
3	CF9	Stable	Stable	Stable
4	PF6	Stable	Stable	Unstable
5	PF7	Stable	Stable	Stable
6	PF8	Stable	Stable	Stable
7	PF9	Stable	Stable	Stable

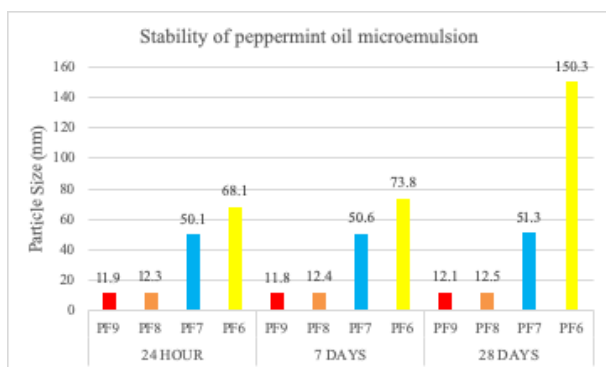


Figure 1: Stability of peppermint oil microemulsion

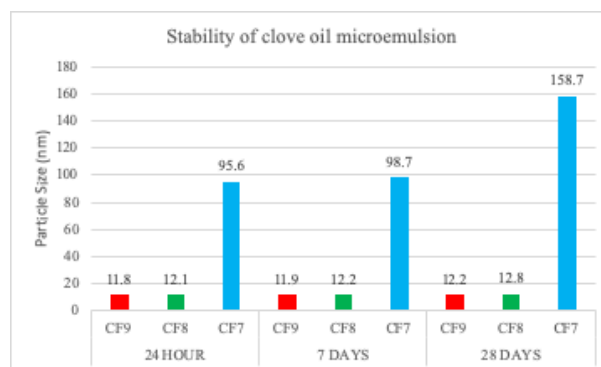


Figure 2: Stability of clove oil microemulsion

RESULTS AND DISCUSSION

Based on the transparency of the prepared formulations, four formulations of peppermint oil and three formulations of clove oil showed transparent clear mixture when observed visually. Transparency increased with the increase in the concentration of surfactant. So these transparent formulations CF7, CF8, and CF9 for clove oil and PF6, PF7, PF8, and PF9 for peppermint oil were considered for further analysis (Table-2)

The particle size of the prepared microemulsions were found to be 68.1nm, 50.1nm, 12.3nm, 11.9nm for PF6, PF7, PF8, PF9 respectively and 95.6nm, 12.1nm, 11.8nm for CF7, CF8 and CF9 respectively. The zeta potential was found to be -25.3mV, -17.7mV, -21.6mV, -20.9mV for PF6, PF7, PF8, PF9 respectively and -20.0mV, -16.5mV, -20.8mV for CF7, CF8 and CF9 respectively.

The pH, viscosity and conductivity of the selected formulations were measured and shown in the Table-4.

No signs of phase separation were seen after centrifuged at 3000 RPM. Also, kinetic stability was achieved over the period of 28 days and found that PF6 and CF7 were not stable for a long period of time as shown in table 4. The particle size of PF6 and CF7 were changed over the period of time which is clearly shown in figure-1 and figure-2.

From the results obtained, it can be verified that the particle size of formulations CF8 and CF9 of clove oil based microemulsion and PF7, PF8 and PF9 of peppermint oil based microemulsions were in the nanometer range. And, from zeta potential measurements we can conclude that droplets of those formulations were stable. Similarly, kinetic stability was established over the period of 28 days and the result showed its stability during the entire period of 28 days.

CONCLUSION

Current scenario demands the delivery of drug to its specific site of action in more prominent and competent way. Microemulsion

as being one of the novel approaches has gained importance due to its stability and physical properties it shows. The use of this novel approach to deliver pharmacologically active natural oils in this study can surely prepare a base research for the upcoming study so we can see a concomitant commercial formulation in near future.

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