P-116	**Fabrication of Delayed Release Gelatin /HPMCP Microparticles Containing Peppermint Oil**	

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INTRODUCTION AND OBJECTIVES

Natural and synthetic polymers have extensively being used for encapsulation of different chemical reagents, food additives and drugs [1]. Micro and macropasules can be highly desirable for treatment of common site specific disease of GI tract including Irritable Bowel Syndrome (IBS) [2] due to many advantages of these systems. Uniform distribution of drug-containing particles and less local damage to the gastrointestinal (GI) mucosa, reproducibility of transport in GI tract and adding controlled release properties to the particulate system are among the most important advantages of particulate delivery systems [3].

Peppermint oil (PO) is an effective therapy for the symptoms of IBS through its relaxation of smooth muscles, carminative, and antibacterial actions. Enteric delivery of PO is crucial for drug therapy, and also for avoiding contact with the gastric mucosa and gastric pH, which decomposes the essential oil [4]. Therefore, providing simultaneous enteric delivery of PO with the particulate delivery systems would be highly desirable. The objective of this study was to develop a simple technique for fabrication of spherical microcapsules for site-specific delivery of PO.

MATERIALS AND METHODS

Peppermint oil (PO, grade BP) was purchased from Zardband Co., (Tehran, Iran). HPMCP (HP-55) manufactured by Shin-Etsu Chemical Co., Ltd. (Tokyo, Japan). Gelatin, sodium hydrogen carbonate and citric acid were purchased from Sigma Chemical Co., (Poole, UK). Also, menthol standard, di-sodium hydrogen phosphate and hydrochloric acid were supplied from Merck (Darmstadt, Germany).

Preparation of microcapsules

An oil in water/precipitation technique was developed for encapsulation of PO in a gelatin/HPMCP mixed polymer system. This new technique adapted from the work reported by Cerdeira *et. al.,* [17] for encapsulation of a model micronized powder. Screening studies using different concentrations of reagents and working conditions were carried out to fabricate the macrocapsules. Briefly, an appropriate amount of PO (Table 1) was emulsified in an alkaline solution (2% w/v $NaHCO_3$) of HPMCP (HP-55) containing different amount of gelatin 45-55% w/w (total polymer 8-12 %w/v) using a magnetic stirrer (500 rpm) for one hour. The resulting emulsion was then added dropwise through a needle (i.d. 1.8mm) to 100 mL of citric acid solution (10%w/v) under mechanical stirring. The resulting macrocapsules were then filtered and dried at room temperature.

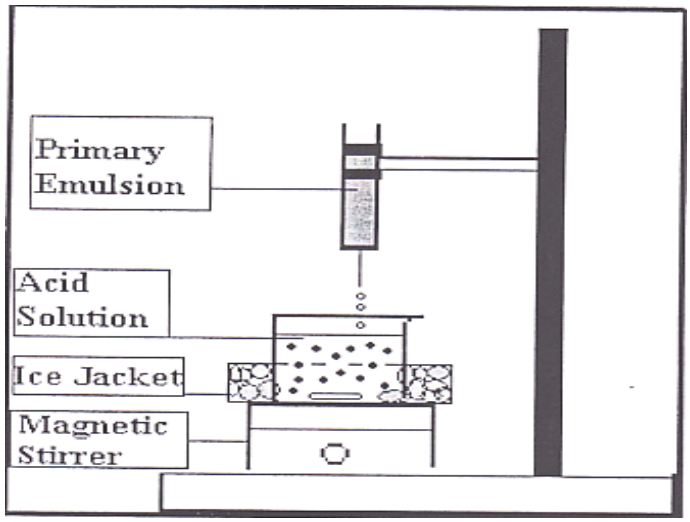

Fig 1- Schematic presentation of microparticle preparation instrument

Determination of loading and encapsulation efficiency

The amount of the encapsulated PO was determined by dissolving a sample of 20 mg macrocapsules in 2 mL NaOH 2N and 2mL hexane which already contained 100 ppm linalool as the internal standard. GC-FID analyses of the oil were conducted using a Thermoquest-Finnigan instrument equipped with a DB-1 fused silica column (30m × 0.25 mm i.d., film thickness 0.25 µm). Nitrogen was used as the carrier gas at the constant flow of 1.1 mL/min. The oven temperature was raised from 60 ºC to 110 ºC at a rate of 5 ºC/min and then to 250 ºC at a rate of 10 ºC/min.

Loading(%) = Weight of Loaded Po × 100 / Weight of Po loaded sample

Encapsulation Efficiency(%) = Loading × TMW (mg) × 100 / added Po(mg)
(TMW = Total Macroencapsule Weight)

Drug release test

Drug release test was performed according to an adapted

procedure [4] from the United States Pharmacopoeia 25, using paddle apparatus.

RESULTS AND DISCUSSION

The results of the optical microscopy (Figure 2) for the PO emulsion, showed that the droplets of PO were poly dispersed in respect of the size range with diameters from less than 5 to more than 50 ∓m. Preparation of macrocapsules by adding the primary emulsion to the acidic medium led to the solid macrocapsules with mean size 1 mm (Figure 3). The resulting macrocapsules were spherical and monodispersed and had no relationship with the PO droplets in the emulsion with the extensive particle size range (Fig. 3). Therefore, the size of the resulting macrocapsules may be attributed to the parameters like needle size, height and the polymer concentration.

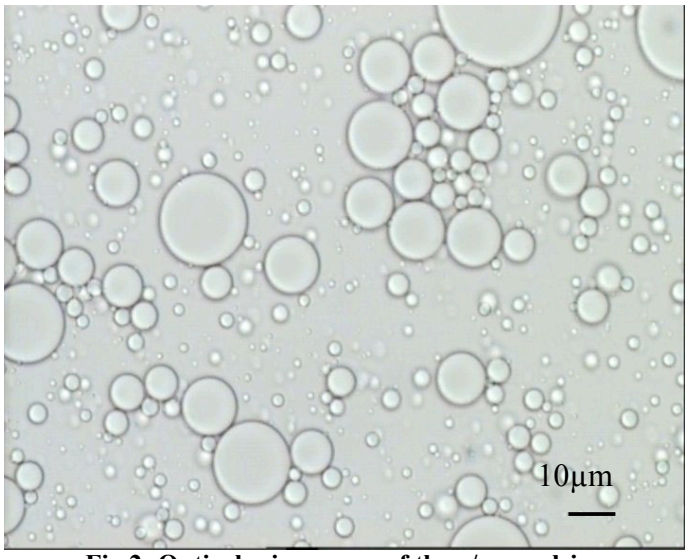

Fig 2: Optical microscopy of the o/w emulsion

The results of drug release test (Fig. 4) showed that microparticles can protect about 70% of loaded PO from acidic conditions of stomach. However, upon exposure to the alkaline pH of intestinal tract, the polymeric matrix release the whole entrapped EO.

CONCLUSION

Simple emulsification/precipitation technique can be used to fabricate gelatin/HPMCP loaded PO macroparticles. These microparticles can control PO release upon different pH conditions of GI tract.

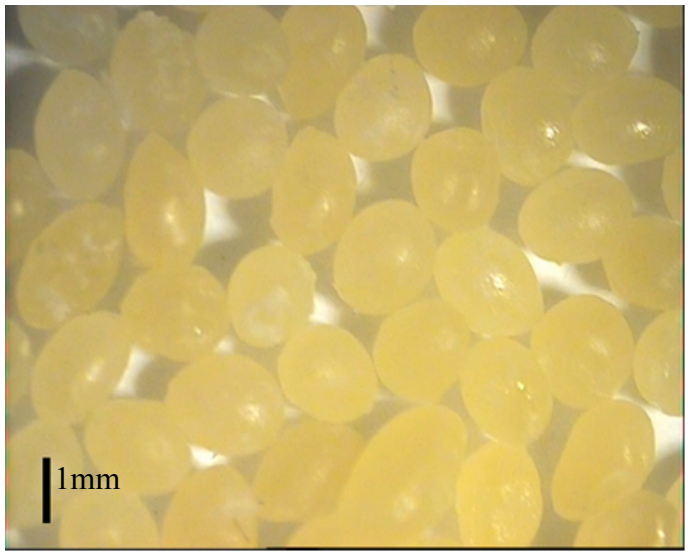

Fig 3: Photograph of the PO loaded macrocapsules

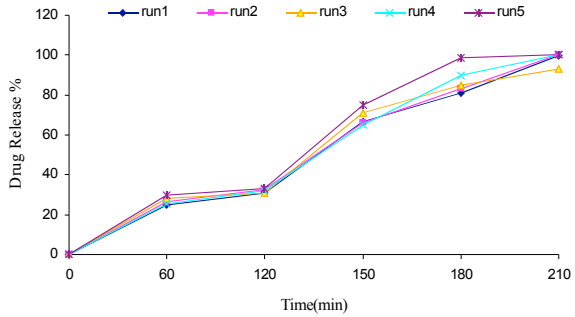

Fig 4: Drug release test in acid (120 min) and buffer (90 min) solutions

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