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FORMULATION AND EVALUATION OF TETRACYCLINE HYDROCHLORIDE MICROCAPSULES BY SOLVENT EVAPORATION METHOD

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Research Article

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ABSTRACT
In the present study microcapsules has been developed by using polymer ethyl cellulose by solvent evaporation method. Tetracyclin hydrochloride was chosen as model drug due to its bitter test and photosensitivity. Microcapsules are prepared by different ratio of thickness of coating layer and core. The prepared microcapsules were evaluated for its partical size, amount of drug entrapped and drug release pattern. The optimized formulation was stable, mask the bitter taste of tetracycline and also found to sustain release of drug as compared to conventional tablet.

KEYWORDS
Microcapsules, Solvent evaporation method, Ethyl cellulose

Introduction

Tetracycline is most important broad spectrum antibiotic, tetracycline hydrochloride is bright yellow, crystalline salt that is stable in air but darkens on exposure to strong sunlight. The hydrochloride salt is used most commonly in medicine. One gram of hydrochloride salt dissolves in about 10 ml of water and in 100 ml of alcohol. Microencapsulation of tetracycline hydrochloride prolongs its action and reduces the number of dosings. It also solves the problem of bitter taste and photosensitivity[1-2]

Microencapsulation is one of the most intriguing fields in the area of drug delivery system. Today, the topic of microencapsulation is extensively studied inside major pharmaceutical companies & universities as well as research institute[3].

It is a technology devoted to entrapping solids, liquids, or gases inside one or more polymeric coatings. Fundamental consideration of microcapsules include Core material, Coating material, Selected stability, release & other properties, Equipment processing, methodology. Various process of microcapsules and their coating and suspending materials are given in **Table no 1**[3-4].

Table No 01: Various processes of microcapsules and their coating and suspending materials

Process	Coating material	Suspended material
Interfacial Polymerisation	Water soluble & insoluble monomers	Aqueous / Organic solvent
Complex coacervation	Water soluble poly electrolytes	Water
Coacervation	Hydrophobic polymers	Organic solvent
Thermal denaturation	Proteins	Organic solvent
Salting out	Water soluble polymers	Water
Solvent evaporation	Hydrophillic Hydrophobic polymers	Aqueous / Organic solvent
Solvent removal	Hydrophillic Hydrophobic polymers	Organic solvent
Spray drying	Hydrophillic Hydrophobic polymers	Air, nitrogen
Phase separation	Hydrophillic Hydrophobic polymers	Aqueous / Organic solvent

SOLVENT EVAPORATION TECHNIQUE

Microencapsulation by solvent evaporation technique is carried out in liquid manufacturing vehicle. Microcapsules coating is dissolved in volatile solvent, which is immiscible with liquid manufacturing vehicle phase. A core material to be microencapsulated is dissolved or dispersed in the coating polymer solution. With agitation a core coating material mixture is dispersed in liquid manufacturing vehicle phase to obtain appropriate size microcapsules. The mixture is when heated (if necessary) to evaporate solvent for the polymer. In the case in which core material is dispersed in polymer solution, polymer shrinks around the core. In the case in which the core material is dissolved in coating polymer solution, matrix type microcapsules are formed. Once all the solvent for the polymer is evaporated a liquid vehicle temp is reduced to ambient temp. (If necessary) with continue agitation. At this stage, the microcapsules can be used in suspension form, coated on to substrate or isolated as powders. Important factors that must be considered when preparing microcapsules by solvent evaporation technique include choice of vehicle phase & solvent for polymer coating, as this choice greatly influence microcapsules properties as well as choice of solvent recovery technique.

The core material may be either water soluble or water insoluble. A variety of film forming polymer can be used. Parameters affecting solvent evaporation include Polymer, mol. Wt. and concentration, polymer crystallisation, type of drug and method of incorporation (solid, liquid, suspension), organic solvent used, type of surfactant in aqueous phase, organic solvent, evaporation temp, rating of stirring. The application of microencapsulation might well include sustained release or prolong action medication, taste masked chewable tablet,

powder and suspension, single layer tablets containing chemically incompatible ingredients and new formulation concept for creams, ointment, aerosols, dressings, lasters, suppositories and injectables[1,2,6].

MATERIAL AND METHODS:

Material: Tetracycline hydrochloride was procured from haffkine ajantha pharmaceutical limited Jalgaon. Ethyl cellulose was procured from U Medica laboratories pvt ltd WAPI Gujarat. Acetone and sodium lauryl sulphate was procured from Jinendra Scientific.

Preparation of microcapsules: Specified amount of polymer was dissolved in 25 mL of acetone. The drug was passed through the sieve no. 100 so as to obtain easily dispersible particle size. Weighed quantity of Tetracycline hydrochloride was dispersed in above polymer phase and it was stirred for 20 min to ensure uniform distribution of drug particles. This polymer- drug dispersion was emulsified with the 100 mL of liquid paraffin containing 1.3% w/v sodium lauryl sulphate with continuous stirring at 1000 rpm using mechanival stirrer (Remi make medium duty) the stirring was continued for further 2 hours to ensure the complete evaporation of acetone.the microcapsules were separated from liquid paraffin by filteration through whatmann filter paper no. 44, washed three times with 50 mL of n-hexene and air dried for 12 hour and stored well. All batches of microcapsules were prepared in the same way.

EVALUATION OF MICROCAPSULES:

Microcapsules were evaluated for physical properties like repose angle by fixed funnel method, bulk density by three tap method, particle size determination by optical microscopy.

1) **Particle size analysis:** The sample of prepared microcapsules was randomly selected and their size was determined using an optical microscope.

2) **Surface topology studies by Scanning Electron Microscopy**: Scanning electron microscopy of the given sample proves the uniform coating of ethyl cellulose over the core material.

3) **In –Vitro Drug Release Studies :** Preweighed quantity of microcapsules equivalent to 100 mg of tetracycline hydrochloride wrer tied in muslin cloth and were placed in basket USP XXll dissolution test apparatus at a rotational speed of 100 rpm mainted at 37±1° in 900 mL of phosphate of pH 7.4. Samples of 5 mL were withdrawn at hourly interval and filtered through whatmann filter paper n.44 replacing the same volume with fresh dissolution medium. After each sampling the drug content was determined in the filtrate after suitable dilution spectrophotometrically at 278 nm. Results are shown in stable and plot % cumulative drug released Vs. time as shown in figure 1.

4) **Drug content determination:** Microcapsules equivalent to 100 mg of Tetracycline hydrochloride were transferred in a flask containing 0.1 N HCl. This was shaken for 24 hour on mechanical shaker for bursting. The filtrate was collected; suitably diluted absorbance was measured at 278 nm. Corresponding drug concentrations were calculated from the calibration plot. From the drug content data % drug encapsulated was determined using formula.

$$\% \text{ drug encapsulated} = \frac{\text{Weight of drug Present in microcapsule}}{\text{Weight in drug used}} \times 100$$

RESULT AND DISCUSSION:

In present work sustained release microcapsules of Tetracycline hydrochloride were formulated using different polymers by emulsion solvent evaporation technique. Various batches prepared with different core: coat ratio were evaluated for physical properties. The microcapsules vary in size range from 138-276mcm. The particle size distribution was uniform and narrow. It was found that percent entrapment of tetracycline hydrochloride was between 74-82% depending on core: coat in – vitro dissolution studies were performed and plot of cumulative percent drug release Vs time was obtained as shown in figure. Drug release followed a biphasic pattern i.e. initial fast release called as burst effect and later on a sustained release which may be due to swelling of coating polymer. The initial fast release of drug may be due to the porous surface of microcapsules. Microcapsules with ethyl cellulose in 1:1 ratio gives better sustained release for 8 hour and about 94.32 % of drug was released at the end of 8 hour. It was found that as polymer concentration increases drug release was found to be retarted. Percent release with respective time in hour in different formulation shown in table no 2.and In – vitro drug release profile of various batches of microcapsules are shown in figure no1.

TABLE No 2: Percent release with respective time in hour in different formulation

Time (hr)	P1	P2	P3	P4
0	0	0	0	0
1	12.76	11.30	21.48	13.93
2	33.57	31.17	48.40	25.07
3	54.57	36.29	64.71	30.87
4	75.27	52.99	72.86	35.71
5	78.12	59.06	90.12	42.87
6	83.82	67.01	94.31	46.31
7	89.70	70.64	97.20	49.71
8	94.32	73.13	99.17	53.72

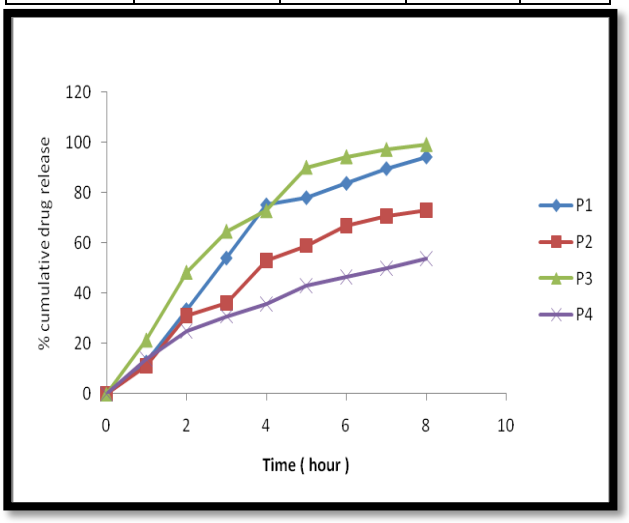

Fig 1:-In – vitro drug release profile of various batches of microcapsules

CONCLUSION:

The ethyl cellulose coated microcapsules of Tetracycline hydrochloride (P1) with core coat ratio 1:1 was found to be spherical, discrete and free flowing and able to sustain the release effectively and may used as oral sustained release multiparticulate system.

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