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FORMULATION AND CHARACTERIZATION OF ETORICOXIB MICROCAPSULES VIA SOLVENT EVAPORATION FOR EMULGEL

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ABSTRACT
This research investigated the formulation and characterization of microcapsules containing a nonsteroidal anti-inflammatory drug (NSAID) through solvent evaporation methods. Microcapsules are widely used in various industries for encapsulating active ingredients, protecting sensitive materials, and controlling release kinetics. This study focused on the preparation and characterization of microcapsules using a solvent evaporation method. Different formulations were investigated, varying in the ratio of core material (NSAID) to shell material (polymers concentration). The influence of these parameters on the morphology, size distribution, and encapsulation efficiency of the microcapsules was systematically studied. Results indicated that formulations with higher polymer concentrations exhibited spherical shapes and higher entrapment efficiencies compared to those with lower concentrations. Optical microscopy was employed to analyze the size distribution of microcapsules, revealing sizes ranging from 50 to 500 µm. Furthermore, the impact of mixing speed during preparation emerged as a critical factor affecting microcapsule shape and size, with slower speeds resulting in potentially less spherical microcapsules.This comprehensive investigation provided valuable insights into the optimization of microcapsule preparation techniques for various applications in drug delivery, cosmetics, and food industries.

Key words: Microcapsules, NSAID, Shell material, Optical microscopy, Cosmetics.

INTRODUCTION
Microcapsules, minute spheres usually ranging from 1 to 1000 micrometers in diameter. Microcapsules attracted significant interest across various disciplines owing to their versatile properties and applications. Microencapsulation is the coating of small solid particles, liquid droplets, or gas bubbles with a thin film of coating or shell material, sealed capsules that can release their contents at controlled rates under specific conditions. Comprising a shell material encapsulating a core substance, these microscale containers offer protection and controlled release capabilities. Efforts are also underway to tailor the release kinetics of encapsulated substances, enabling precise control over the timing and rate of release. This fine-tuning is crucial for applications in drug delivery, where maintaining therapeutic levels of medication in the body over extended periods is essential for efficacy and patient comfort [4]. Furthermore, the utilization of microcapsules extends beyond pharmaceuticals, with emerging applications in cosmetics, food, agriculture, and electronics.

Microcapsules are extensively used in pharmaceuticals for controlled drug delivery. They can encapsulate drugs, protecting them from degradation and allowing for sustained release at predetermined rates, enhancing drug efficacy and patient compliance. In the cosmetic industry, microcapsules are employed to encapsulate active ingredients such as vitamins, antioxidants, and fragrances. This allows for their controlled release upon application, providing longer-lasting effects and improved product performance. These applications demonstrate the versatility and significance of microcapsules across industries, offering tailored solutions to various challenges and driving innovation in material science and technology.

For example, in cosmetics, microcapsules can deliver active ingredients such as vitamins and antioxidants, enhancing product effectiveness and longevity [1]. In agriculture, they can be used for targeted delivery of fertilizers or pesticides, minimizing environmental impact, and optimizing resource utilization [2]. In the electronics industry, microcapsules offer opportunities for self-healing materials, where microcapsules containing healing agents can rupture upon damage, releasing restorative compounds to repair the material as research in microcapsule technology progresses, it continues to unlock new possibilities across diverse industries, driving innovation and addressing pressing challenges with creative solutions. With ongoing advancements in material science, manufacturing techniques, and application-specific customization, microcapsules are poised to play an increasingly pivotal role in shaping the future of various fields.

MATERIALS AND METHODS

MATERIAL: Etoricoxib (East African Overseas, India), 2hydroxy propyl-beta cyclodextrin (East African Overseas, India), Chloroform (Merck international, Ahmedabad), Tween 80 (Swadesh life science, Ahmedabad).

METHODS

Microcapsules of the NSAID drug were prepared using the solvent evaporation method: Microcapsules were created via conventional solvent evaporation at room temperature (25-27°C). Polymer and the drug were dissolved in a volatile organic solvent to form Solution A, while Solution B consisted of water with Tween 80 (0.1%). Droplets of Solution A were added to Solution B, stirred at 200 rpm until solvent evaporation yielded microcapsules. These were then dried in a vacuum desiccator. Table 1 for excipient details [9].

Table 1: Microcapsules formulation of NSAID

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Etoricoxib	10g	10g	10g	10g	10g	10g	10g	10g	10g
2hydroxy propyl-beta cyclodextrin	10g	20g	30g	-	-	-	-	-	-
Ethyle cellulose	-	-	-	10g	20g	30g	-	-	-
Polyvinyl alcohol	-	-	-	-	-	-	10g	20g	30g
Dichloromethane	50ml	50ml	50ml	-	-	-	-	-	-
Chloroform	-	-	-	50ml	50ml	50ml	-	-	-
Acetone	-	-	-	-	-	-	50ml	50ml	50ml

Evaluation of microcapsules.

Release rate of NSAID: NSAID (Etoricoxib) microcapsules coated by different polymers were filtered, washed with distilled water, and lightly blotted to remove excess surface moisture. Subsequently, 1 gram of the microcapsules was introduced into a release cell containing 100 mL of methanol and placed in a sonicated bath at 28°C. At regular intervals, 10 mL of the sample was extracted using a syringe, filtered with filter paper, and its absorbance was measured using a pre-

calibrated UV-spectrophotometer. Fresh methanol was replenished in the cell to maintain a constant volume of the continuous phase. The procedure was executed to discover the encapsulation efficiency (%) and cumulative release rate (%) of the NSAID(Etoricoxib).

Encapsulation efficiency: It indicated how effectively an active ingredient (AI) as a core material has been encapsulated inside the Coating material. It measured the percentage of core material present in the microcapsules and mathematically expressed as:

$$Encapsulation\ efficiency = \frac{Amount\ of\ drug\ entrapped}{Total\ amount\ of\ drug\ added} \times 100$$

Calculation of cumulative release (%): In release rate experimental studies, the concentration of NSAID released from microcapsules at time (t) was assessed using the observed wavelength in a standard calibration curve of UV absorption for the sample drug in a methanol solvent system. This release rate is mathematically represented as:

$$CDR\% = \frac{Drug\ released\ from\ microcapsules\ at\ time}{Total\ amount\ of\ drug\ entrapped\ in\ microcapsues \times 100}$$

Microcapsules particle size distribution by optical microscopic: The optical microscopic method for measuring particle size distribution involves mounting an emulsion or suspension sample on a ruled slide on a mechanical stage. A microscope fitted with a micrometer in the eyepiece was used to estimate particle sizes by comparing them to the scale on the micrometer. Multiple areas of the sample were observed, and particle sizes were recorded. Data was analyzed to create a particle size distribution, and results were validated and reported. While simple and quick, this method may have limitations compared to more advanced techniques.

Scanning electron microscopy analysis: Microcapsule samples were coated with gold particles for enhanced conductivity and imaging quality, then observed at various magnifications using a scanning electron microscope (SEM). This process allowed detailed examination of microcapsule morphology and size, providing valuable insights into their structural characteristics at a microscopic level [8]. The specific SEM model used ensured precise and detailed observations.

RESULTS

Determination of encapsulation efficiency and cumulative drug release: Encapsulation efficiency was observed 66.2% to 94.1% while cumulative drug release was obtained 54.20% to 78.72% in 180 minutes. Table 2 represents encapsulation efficiency and cumulative drug release. Figure 1 represents cumulative drug release of formulations at different time intervals.

Table 2: Encapsulation efficiency and Cumulative drug release

Formulation code	Encapsulation efficiency (%)	% CDR
F1	66.2	54.21
F2	79.3	71.33
F3	82.9	78.72
F4	74.5	71.80
F5	86.3	77.33
F6	94.1	78.56
F7	65.6	69.1
F8	76.8	73.1
F9	81.5	79.2

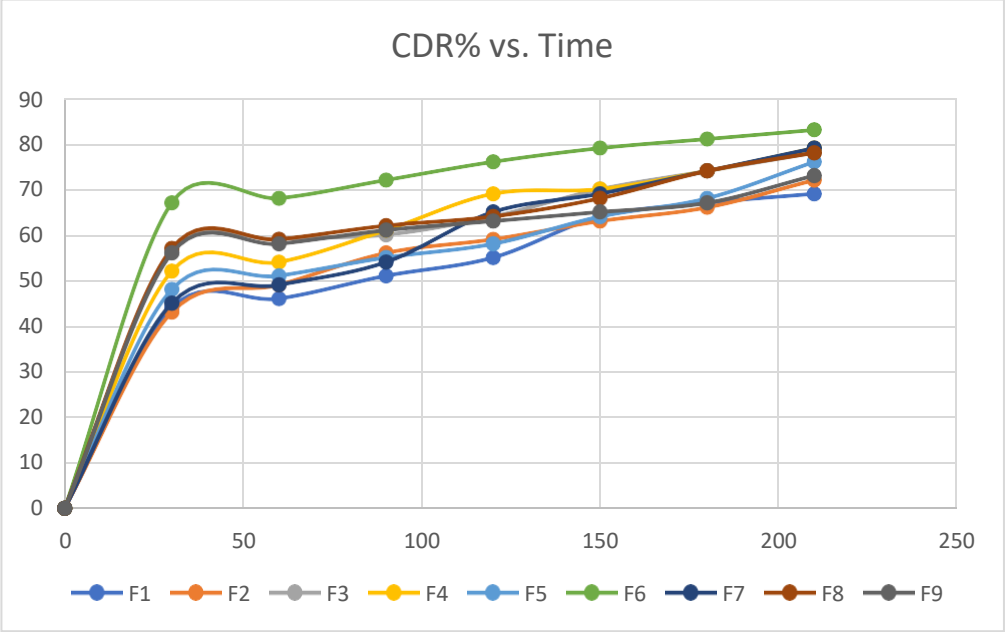


Figure 1: Cumulative drug release of Microcapsules formulations.

Microcapsules particle size distribution by optical microscopic: Table 3 represented average particle size of microcapsules formulations. Figure 2 depicted the graph of size distribution of microcapsules by optical microscopy method. Size ranges between 50-500 µm. Figure 3 showed the illustration of microcapsules in optical microscope.

Table 3: Average particle size of microcapsules formulations.

Formulations code	Polymers	Drug: Polymer	Average particle size (µm)
F1	2hydroxy propyl-beta cyclodextrin	1:1	371
F2	2hydroxy propyl-beta cyclodextrin	1:2	337
F3	2hydroxy propyl-beta cyclodextrin	1:3	334
F4	Ethyle cellulose	1:1	445
F5	Ethyle cellulose	1:2	293
F6	Ethyle cellulose	1:3	227
F7	Polyvinyl alcohol	1:1	477
F8	Polyvinyl alcohol	1:2	301
F9	Polyvinyl alcohol	1:3	278

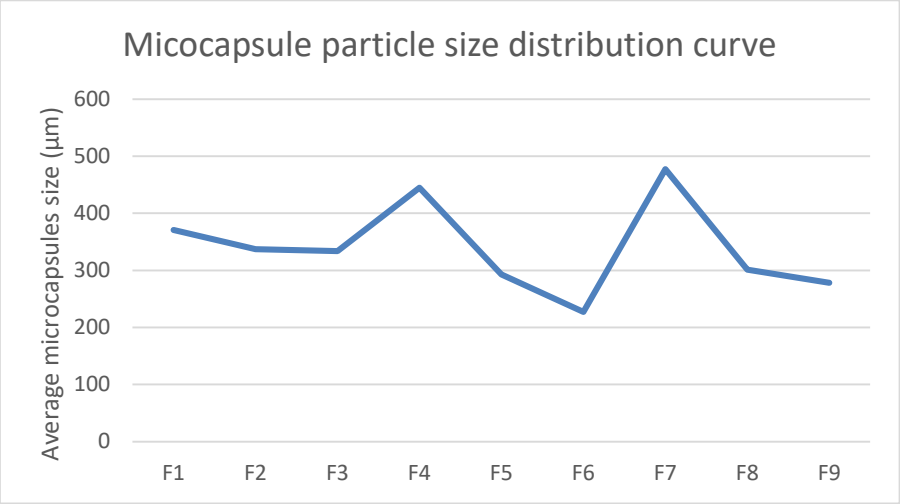


Figure 2: Microcapsules particle size distribution by optical microscopy

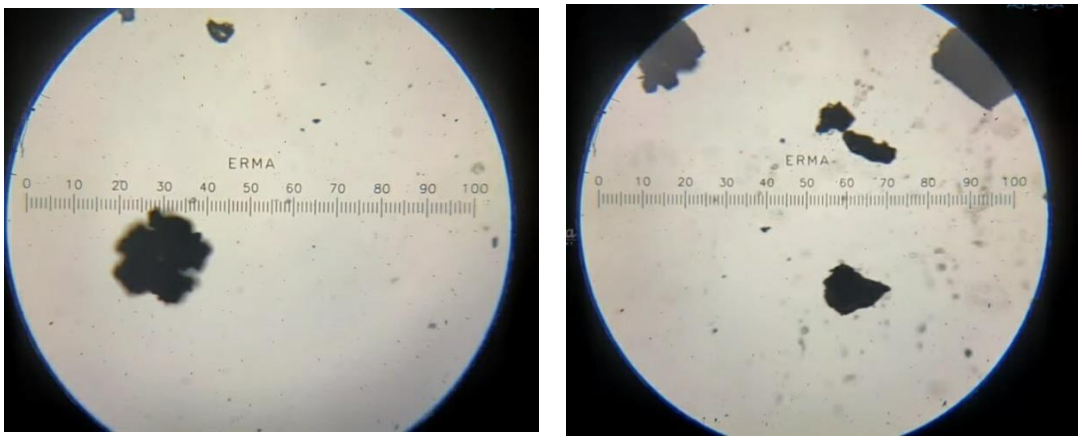
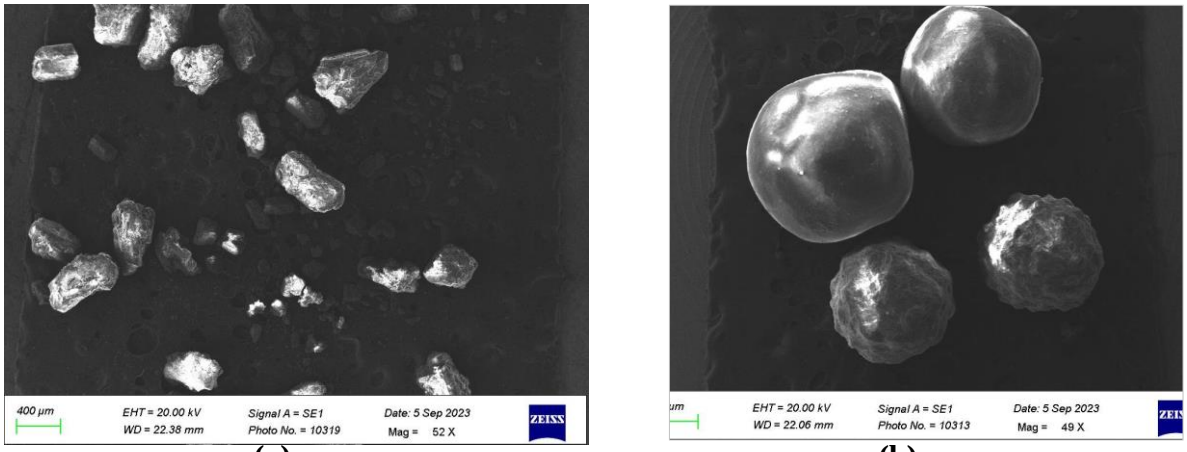


Figure 3: Images of Microcapsules in stage micrometer of optical microscope

Scanning electron microscopy analysis: Figures 4 depicted the morphology of NSAID microcapsules which illustrates non-spherical microcapsules, likely due to a lower quantity of polymers (a) and exhibited spherical shapes without separations duo to higher polymer concentrations (b).



(a) **(b)**

Figure 4: (a) F1 (1:1 of drug and 2hydroxy propyl-betacyclodextrin, (b): F6 (1:3 of drug and ethyl cellulose)

DISCUSSION

This method leveraged the emulsification process, choice of volatile solvents, and the surfactant Tween 80 to ensure uniform dispersion, prevented aggregation, and achieved successful microcapsule formation for NSAID delivery. Allowed the emulsified mixture to undergo solvent evaporation. The highly volatile solvents (chloroform, acetone, dichloromethane) facilitated rapid evaporation, prevented microcapsule aggregation during formation. Used Tween 80 as an emulsifier to stabilize the emulsion formed by combining the shell and core phases. This reduced interfacial tension and promoted uniform dispersion. Higher polymer concentrations in formulations correlated with increased entrapment efficiency, indicating more effective encapsulation of the NSAID within the polymer matrix. Insufficient polymer quantity led to incomplete coverage of the NSAID. As a result, this suggests that different ratio of drug and polymer concentration from F1 to F9 led to improvements in both the spherical shape of the microcapsules and their entrapment efficiency. F6 showed the best overall performance in terms of both characteristics, while F1 exhibited the poorest performance. Adjusting the for microcapsules, particularly the polymer concentration, can significantly impact the quality and effectiveness of the microcapsules for drug delivery applications. Organized the dataset into size bins or ranges (e.g., 50-100 µm, 100-200 µm, etc.). Microcapsules formed at slower mixing speeds may exhibited potentially less spherical shapes compared to those formed at higher mixing speeds. This could be due to reduced shear forces and less uniform distribution of the encapsulated material, leading to irregularities in shape.

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