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Formulation & Evaluation of Nimesulide Bio-Micro Dwarfs using A Novel Bio-retardant from the Rhizomes of *Zingiber officinale*

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Abstract : The current aim of our research work is to isolate bio-polymer from fresh rhizomes of *Zingiber officinale* & to evaluate its retardibility by formulating microdwarfs containing nimesulide as a model drug. The bio-material was isolated by a simplified method. Six different bio-micro dwarf formulations were prepared using isolated bio-material as a retardant. The formulated microcapsules were evaluated for flow property & in –vitro release studies.
Our research result revealed that the isolated bio-material showed promising readability for a period of 7 hours. Finally the conclusion was drawn that the bio-material can serve as a potential bio-retardant
Key words: Nimesulide Bio-Micro Dwarfs, Nimesulide, Bio-retardant, *Zingiber officinale,* Rhizomes.

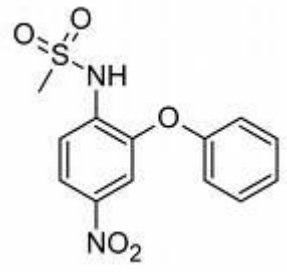
Introduction and experimental

Microparticulate drug delivery system is one of the processes to provide the sustained & controlled delivery of drug to long periods of time. They are small particles of solids or small droplets of liquids surrounded by walls of natural & synthetic polymer films of varying thickness & degree of permeability acting as a release rate controlling substance & have a diameter upto the range of 0.1µm-200µm [1]. Microparticles have been proved to be an ideal way of preparing sustained & controlled release dosage forms. They are also a beneficial way of delivering APIs which are pharmacologically active but are difficult to deliver due to limted solubility in water. In such drugs the attainment of high Cmax, Tmax, and Area under the curve is problematic. Thus a need exists for immediate release products containing these agents[2]. Microparticles provide effective delivery of agents that are insoluble or sparingly soluble in water. The formulations of microparticles also provide the method of targeting the drug delivery to specific sites. Application of microparticles include sustained or prolonged action medication , taste- masked chewable tablets , powders & suspensions , single layer tablet comtaining chemically incompatible ingredients & new formulation concepts for creams , ointments , aerosols , dressings , plasters , suppositories & injectables[3].Microsphere-based formulations can be formulated to provide a constant drug concentration in the blood or to target drugs to specific cells or organs[4,5].

The coating material can be selected from a wide variety of natural and synthetic polymers depending on the core material to be encapsulated and the desired characteristics. The amount of coating material used ranges from 3% to 30% of the total weight, which corresponds to a dry film thickness of less than 1–200 µm, depending on the surface to be coated. The coating material should be capable of forming a film that is cohesive with the core material, be chemically compatible & non reactive with core material such as strength, flexibility, impermeability, optical properties & stability[3]. Some examples of natural and synthetic hydrophilic polymers used are[6,7,8] are agar acrylic polymers, polyacrylic acid, poly acryl methacrylate, gelatin, poly(lactic acid), pectin(poly glycolic acid), waxes(poly hydroxyl butyrate-co-valerate), cellulose derivatives, cellulose acetate phthalate, Nitrate, Ethyl

cellulose, Hydroxy ethyl cellulose, Hydroxypropylcellulose,Hydroxypropyl methyl cellulose, Hydroxypropylmethylcellulose phthalate,Methylcellulose,Sodiumcarboxymethylcellulose,Poly(orthoesters),Polyurethane,Poly(ethylene glycol), Poly(ethylene vinyl acetate), Polydimethylsiloxane, Poly(vinyl acetate phthalate), Polyvinyl alcohol, Polyvinyl pyrrollidone,shellac.

Nimesulide (NIM) is described chemically as *N*-(4-nitro-2-phenoxyphenyl) methane sulfonamide. It is a unique non-steroidal anti-inflammatory (NSAID) agent) with analgesic properties having specific affinity to inhibit cyclooxygenase-2 enzyme. It is highly effective in reducing pain associated with osteoarthritis, rheumatoid, and other degenerative joints disorders, low back pain, dysmenorrhoea, gynaecological condition, thrombophlebitis, dental pain and inflammations etc.



Anti-inflammatory action may be exerted by reduced generation of superoxide by neutrophill & inhibition of platelet activating factor (PAF) & tumour necrosis factor release (TNF) release[9]. Ginger consists of rhizomes of *Zingiber officinale* Roscoe, family Zingiberaceae. The objective of this work is to isolate bio-material from fresh rhizomes of *Zingiber officinale* & to evaluate its retardibility by formulating microdwarfs containing nimesulide as a model drug. The isolated bio-material was subjected for various physico chemical parameters like colour, odour, solubility, particle size, & IR spectral studies. Six different microdwarfs were formulated by non-solvent addition method using different ratio of isolated bio-material as a retardant & nimesulide as a model drug (i.e. drug polymer ratio of 1:1, 1:2, 1:3, 1:4, 1:5, 1:6) with other co-processants. The isolated bio-polymer show good solubility in water, with colour changing point at 165-170°C. The formulated microcapsules were evaluated for flow property, particle size, shape, entrapment efficacy & in –vitro release studies.

Materials-

The model drug Nimesulide was supplied as gift sample by APS Biotech Pvt. Ltd Roorkee. All the reagents were of analytical grade. Double distilled water was used throughout the experiment.

Isolation of the bio-polymer from *Zingiber officinalis* rhizomes: 250 gm of the fresh ginger was grinded in pestle mortar. 500 ml of double distilled water was added .and subjected for stirring using a mechanical stirrer at 2000 rpm for the period of one hour. The mixture was filtered through a muslin cloth & further subjected for centrifugation at 2000 rpm for 20 minutes. The supernant liquid was pooled & treated with double the quantity of acidified methanol with constant stirring. The mixture was subjected for cooling for 12 hrs. The bio-material was separated by centrifugation at 4000 rpm. The mixture was dried at dessicator for the period of 12 hours. The bio-material was powdered & screened through sieve no. 200.

Formulation of bio- microdwarfs

Bio-microdwarfs were formulated using Nimesulide as model drug, bio-material as a retardant & encapsulating wall material. The all bio-microdwarfs were formulated by non-solvent addition method. The different drug & polymer: ratio (1:1, 1:2, 1:3, 1:4, 1:5, 1:6) were used & six different formulations were prepared.

The formulation of Nimesulide microparticles was done by preparing aqueous solution of 100mg bio-material by sonication for about 15 min. To this sol about 100 mg of lactose was added as anti-aggregant agent. Nimesulide was dissolved in alcohol which acts as a non-solvent for the polymer & added in above mixture with constant stirring & microdwarfs were collected by centrifugation at 3000 rpm for 20 minutes. Microdwarfs were further dried & screened through sieve no. 120.

TABLE-1 FORMULATIONS OF BIO-MICRODWARFS

S.NO.	FORMULATION	ZM1	ZM2	ZM3	ZM4	ZM5	ZM6
1.	Drug:Bio polymer ratio	1:1	1:2	1:3	1:4	1:5	1:6
2.	Bio-polymer(mg)	100	200	300	400	500	600
3.	Nimesulide(mg)	100	100	100	100	100	100
4.	Lactose(mg)	100	100	100	100	100	100

Particle shape & size. All formulations were subjected for particle size distribution study by optical microscopy method.

Entrapment efficiency - Drug entrapment efficiency was calculated by dissolving microparticles equivalent to 5 mg of drug in a small quantity of methanol. The solution was filtered through Whatman filter paper no. 41, suitably diluted & absorbance was measured using UV spectrophotometer.

***In vitro* Dissolution studies -** The Dissolution rate studies of formulated bio-microdwarfs were performed in triplicate using a dissolution apparatus using basket type USP Type I. The Study was conducted for a period of 8 hours first 2 hours in PH 1.2 followed by adjustment to PH 7.4 for a period of 6 hours at 37ºC. 5 ml of samples were withdrawn at every 30 min. & fresh buffer was replaced to adjust the volume of dissolution medium. The withdrawn samples were suitably diluted & filtered through 0.45 µm & analyzed spectrophotometrically (schimadzu) at λmax 450 nm.

Results & discussions.

Physical properties of isolated bio-material from *Zingiber officinale* rhizomes

Table 2 illustrates the various physical properties of isolated bio-material.

Table 2 Physical properties of isolated bio-material

1.	COLOUR	Reddish brown
2.	ODOUR	characteristic
3.	SIZE	irregular
4.	TASTE	slightly bitter
5.	SOLUBILITY	Slightly soluble in water
6.	COLOUR CHANGING POINT	165-170°C

IR Spectra of the isolated bio-material

The IR spectrum of the polymer is depicted in fig 1.

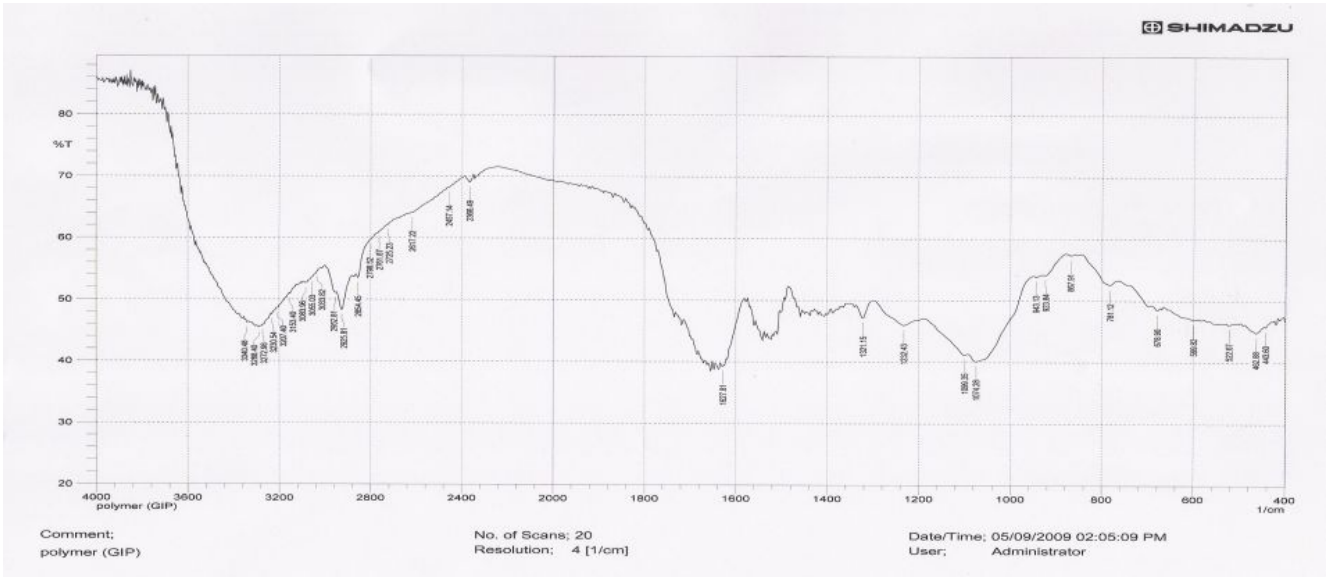


Fig 1 IR Spectra of isolated bio-material

Particle size studies

The particle size of different formulations was found to lie between 169-179 µm. Fig2 shows the bar graph of different formulations

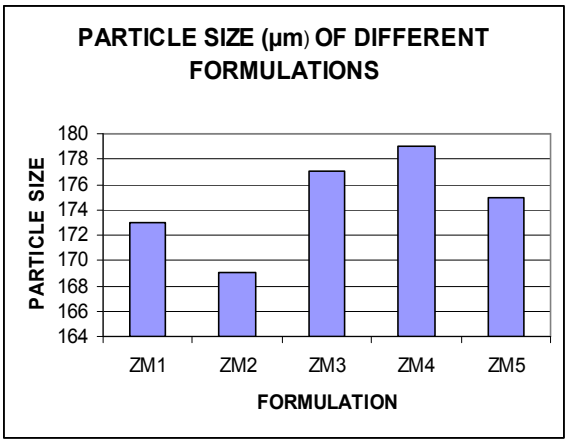


Fig 2 particle size of different formulations

Entrapment efficacy

The Percentage drug content of various formulations was found to be in between 74.34-83.82%. Figure 3 illustrates the bar graph representation of drug content of various formulations.

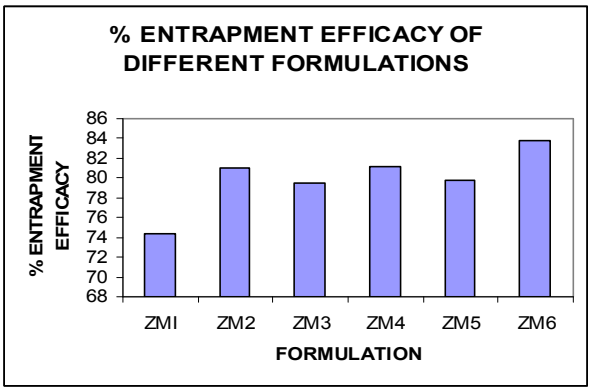


Fig 3 drug content of various formulations

***In vitro* release profile of the formulated microdwarfs**

The *in-vitro* dissolution study of formulated bio-microdwarfs has displayed significant prolonged release for a period of 8 hours. The best formulation ZM3 was selected as a best bio-microdwarfs formulation by comparing its t50 & t80 value with other formulations. The release data was subjected for various mechanisms like 0 order, first order & higuchi model in order to evaluate release kinetics of different formulation. All formulation show 0 order release pattern with a diffusion mechanism.

Figure 4 represents the release rate curves of the different formulation

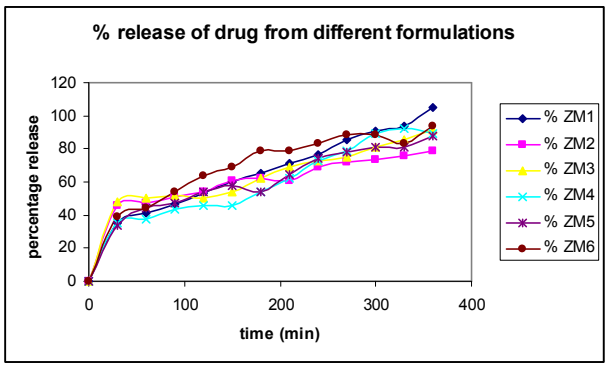


Fig. 4. Release rate curve of different formulations

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