Thus dispersible tablets of ibuprofen could be formulated employing Primogel as internal and external disintegrant and also with Potato starch as internal Primogel and PGS as external disintegrants. These tablets fufilled all official (I.P) requirements of dispersible tablets and gave rapid and higher dissolution rates and dissolution efficiency values than the conventional tablets. Dissolution rate of ibuprofen, a poorly soluble drug, could thus be increased by formulating it as dispersible tablets.

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# Preparation and Evaluation of Submicron Cellulose Particulate System Containing Etoposide


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**Cellulose derivatives have been used to prepare nanospheres entrapping the drug etoposide. Adopting the technique of desolvation for nanosphere formation, discrete spheres have been obtained, as observed by transmission electron microscopy. Study on *in vitro* release profile of sample batches showed bi-phasic release pattern.**


Some of the unique features like satisfactory stability, easy preparation, possibility of reducing toxicity and elevating the therapeutic efficacy, make nanoparticle a suitable drug-delivery system for targeted distribution of anti-cancer drugs[1]. Nanoparticles containing cytotoxic agents could be useful for the treatment of certain cancers that often show resistance to the uptake of free drug[2]. The feasibility of this approach was demonstrated by many of the investigators and many of the applications to which liposome have been put, await investigation using nanoparticles[3]. Tissue biocompatibility of cellulose derivatives has been studied recently[4].

In our present study, we have made an attempt to identify the suitability and potentiality of ethyl and methycellulose as a natural carrier for anticancer drugs through their *in vitro* release characteristics. The preliminary investigation on release characteristics of this system may enable to justify its *in vivo* application in targeted distribution of anti cancer drugs. Hence, discrete and uniform nanospheres containing etoposide have been prepared from ethyl and methylcellulose by modified desolvation method. The drug loading capacity and *in vitro* release characteristics of these nanospheres were studied.

Etoposide B.P. was obtained from Cipla, Bangalore. Ethyl cellulose 20,064-6 and methylcellulose 27,444-5 were purchased from Aldrich Chemicals, USA. Other reagents like sodium sulfate anhydrous, ethyl acetate and sodium phosphate were of analytical grade.

Nanospheres were prepared by modified desolvation method reported previously by Mukherji et al[5], where


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50 ml of an ethanolic solution containing various amount of etoposide and tween 80 (1% w/v) was desolvated by stirring at 800 rpm and 30 ± 1° using distilled water and 1% w/v of ethyl cellulose. The resultant turbid dispersion was again stirred vigorously at 800 rpm for 10 min and dried at 30° by applying it as a thin film on glass plates. Ethyl cellulose nanospheres were obtained in the form of flaky masses. By following the same method three batches of ethyl cellulose nanospheres were prepared but the amount of etoposide added was varied with each batch, which was 20 mg, 30 mg, and 40 mg respectively, for $EC_2$, $EC_3$, and $EC_4$ batches.

Methyl cellulose nanospheres were prepared by desolving 50 ml of 1% w/v of methyl cellulose in distilled water containing various concentration of etoposide and 0.5% w/v of tween 80 with 5% w/v of solution of sodium sulfate as desolving agent at 25 ± 1°. The extent of desolvation was controlled by absorbance measurements at 550 nm. The resultant turbid dispersion was again stirred vigorously at 860 rpm for 10 min and dried at 30°. Methylcellulose nanospheres were formed together with coarse particles which were removed by controlled filtration. By following the same method, three batches of methyl cellulose nanospheres were prepared, but the amount of etoposide added in each batch was varied, which was 20 mg, 30 mg and 40 mg respectively for $MC_2$, $MC_3$ and $MC_4$ batches.

The average particle size of nanospheres in each batch was determined by measuring diameter of all the sphere and the magnification factor was calculated using a transmission electron microscope[6].

Fifty milligrams of nanospheres from each sample batch $EC_2$, $EC_3$ and $EC_4$ were taken in three different conical flasks and dissolved in 10 ml of ethyl acetate. The solution was centrifuged at 5000 rpm for 15 min. The supernatant solution was separated and analysed by a HPLC method.

Ten milligram of nanospheres from each sample batch, $MC_2$, $MC_3$ and $MC_4$ were taken in three different conical flasks and dissolved in 8 ml of ethyl cellulose and the solution was centrifuged at 5000 rpm for 15 min. The supernatant solution was taken and analysed for the drug content by a HPLC method.

The drug estimation was done by following a previously reported HPLC assay procedure[7]. An HPLC model 484 (Waters Inc. USA) was used for this purpose, using phenyl column. The column has 3.9 mm internal diameter and was 300 mm in length. It was packed with 10 µm particles of silicagel chemically loaded with phenyl group. The mobile phase was dilute glacial acetic acid (1:100) containing 6.44 g sodium sulphate in 1000 ml. The flow rate was adjusted so that a retention time of 20 min for etoposide was obtained.

This study was carried out according to the procedure described by Kim *et al*[8]. Etoposide loaded nanospheres (50 mg) were taken from each batch ($EC_2$, $EC_3$, $EC_4$, $MC_2$, $MC_3$, $MC_4$) in a 250 ml conical flask and 100 ml of isotonic normal saline was added. The flask was kept in a shaker cum incubator maintained at 37°. Five millilitre sample were withdrawn at various time intervals and replaced by the same volume of isotonic normal saline. Each sample was filtered through a membrane filter of pore size 0.2 to 0.45 µm under vacuum. The drug content was estimated by high performance liquid chromatograpy (HPLC Water's model 484). The samples were withdrawn after 0, 0.5, 1, 2, 4, 8, 16 and 24 h.

Fig. 1 shows the transmission electron micro graph of ethyl cellulose nanospheres. The particles are spherical, discrete and regular with the size ranging from 122 to 648 nm with an average size of 286 nm. The drug loading capacity of $EC_2$, $EC_3$ and $EC_4$ batches were found to be 6, 9 and 11.2 µg/mg respectively. The payload of etoposide per mg of nanosphere increase as the drug polymer ratio is increased. Fig. 2 shows the *in vitro* release study of $EC_2$, $EC_3$ and $EC_4$ batches. A bi-phasic

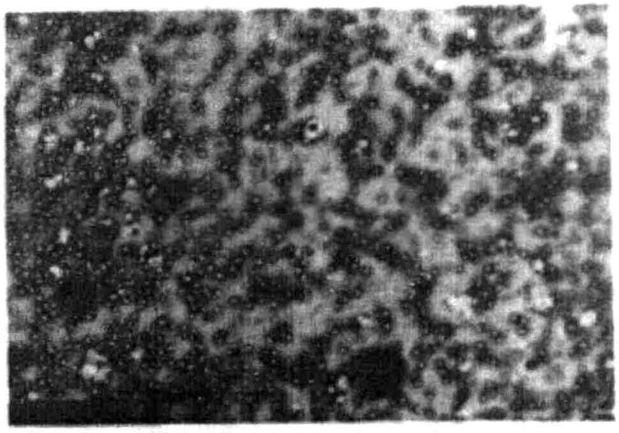

**Fig. 1 : Shows theTEM of Ethyl cellulose nanosphere containing Etoposide (Magnification - 11 000)**

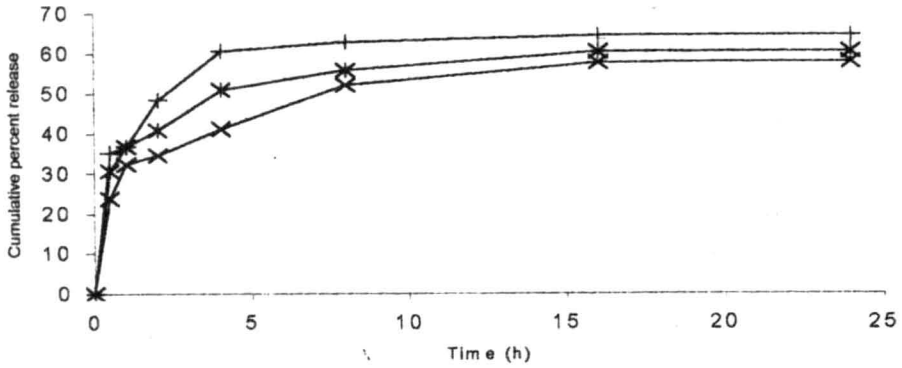


**Fig. 2: *In vitro* release pattern of ethyl cellulose nanospheres containing Etoposide**
**Etoposide loaded nanospheres (ethyl cellulose) EC2 (+), EC3(x) and EC4(✱) were incubated in isotonic normal saline (37°). Samples withdrawn at different time intervals and etoposide was determined by HPLC**

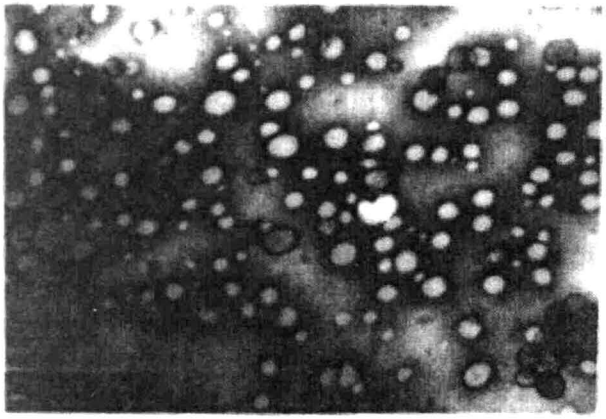

**Fig. 3: Shows the TEM of Methyl cellulose nanosphere containing Etoposide (Magnification - 3600)**

release pattern was observed with an initial burst effect after 0.5 h. Fig. 3 shows the transmission electron micrograph of methylcellulose nanospheres. The particles are spherical, discrete and regular with an size ranging form 256 nm to 1.2 μm with an average size of 452 nm. The payload of Etoposide per mg of nanosphere was found to be 17.7, 19.6 and 24.2 μg/mg respectively for $MC_2$, $MC_3$ and $MC_4$ batches. Fig. 4 shows the release of etoposide in a bi-phasic pattern with an initial burst effect after 0.5 h.

It has been observed that the playload of etoposide per mg of nanosphere in both ethyl cellulose and methylcellulose increased as the drug/polymer ratio increases. But the drug loading capacity of methyl cellulose nanospheres was relatively higher than the ethyl cellulose nanosphere, it could be due to the affinity of

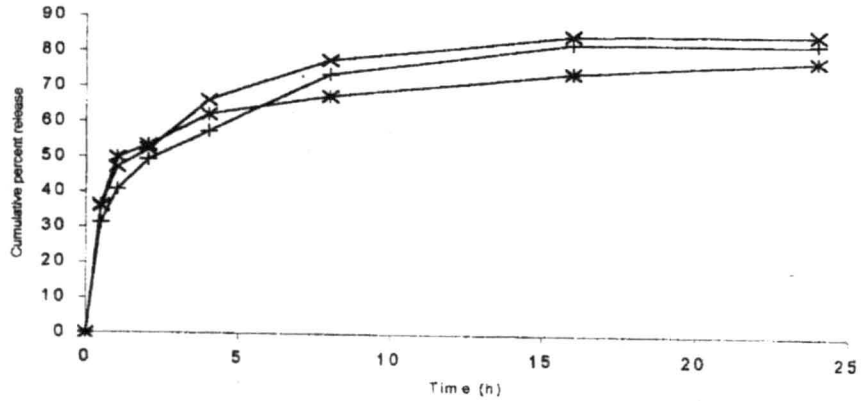


**Fig. 4: *In vitro* release pattern of methyl cellulose nanospheres containing Etoposide**
**Etoposide-loaded nanospheres (methyl cellulose) MC2 (✱), EC3(+) and EC4(x) were incubated in isotonic normal saline (37°). Samples withdrawn at different time intervals and etoposide was determined by HPLC**

lipophillic drug towards hydrophillic polymer, as it has been proved for some hydrophillic drugs like doxorubicin with higher affinity towards natural hydrophillic polymers.

In the *in vitro* release study of both ethyl cellulose and methyl cellulose nanospheres, the initial burst is considered to be due to the release of the drug located on the particle surface, and the second part of the release profile could be due to the drug diffusing out of the polymer particles and the breakdown of polymeric material. The same phenomenon has been observed by Gurny *et al*[9]. for PLA nanospheres containing testosterone.

This study has shown that distinct and discrete nanospheres containing etoposide can be prepared from ethylcellulose and methylcellulose and the drug entrapment efficiency of methylcellulose is relatively more than the ethylcellulose. The *in vitro* release profile of drug from both the polymers indicates their potentiality and suitability for targeted distribution of anti-cancer drugs. However, a thorough stability analysis and *in vivo* drug distribution of these nanospheres are yet to be established.

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# Antibacterial and Antifungal Activities of Marine Sponges


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**Free fatty acid mixtures obtained from the hydrolysis of lipids isolated from seventeen marine sponges collected from the Orissa coast were screened against selected human pathogenic bacteria and fungi. The fatty acid components of two species, *Plakina monolopha* and *Callyspongia sp.* showed antibacterial activity against *Vibrio cholerae* and *Pseudomonas aeruginosa* while the fatty acid components of *Callyspongia sp.* showed antifungal activity against *Candida albicans*. These components have not shown any inhibitory activity against the useful human intestinal bacterium *Bacillus laterosporus*.**


Marine sponges have been reported[1-8] earlier as a source of lipids, glycolipids, phospholipids and corresponding long chain saturated and unsaturated fatty acids besides other novel compounds. Fatty acids obtained from marine algae have shown antimicrobial activity[9,10] and fatty acids from Caribbean sponges have been reported earlier to possess antifungal activity[11]. Hence, an attempt is made to investigate the antibacterial and the antifungal activities of free fatty acid components of 17 marine sponges collected from the Orissa coast[12] by SCUBA divers from a depth of 25-30 m. Two out of 17 sponges, *Plakina monolopha* (family: Halinidae) and *Callyspongia sp.* (family: Callyspongidae) showed activity and the results are presented in this paper (Table-1).


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