leading to a continued and more efficient fibrinolysis in the absence of a generalized proteolysis in the circulation," the scientists have reported.

Sahni's group have used recombinant DNA technology to design and construct several clot-specific, delayed-action derivatives of second-generation streptokinase. According to Sahni, detailed biochemical studies using these purified derivatives have shown that they can successfully activate human plasminogen at rates comparable to those of natural streptokinase, but after variable lag periods (10 to 20 minutes, depending on the construct) *in vitro*.

Fibrin clot lysis experiments in human plasma have shown that these derivatives are active under physiologically relevant conditions — they retain their ability to initiate clot dissolution after latent periods that are similar to those obtained for plasminogen activation *in vitro*, the scientists say.

"The development of novel, recombinant clot-specific forms of streptokinase through protein engineering exemplifies the successful application of [recombinant DNA technology] to the design of potentially useful second-generation derivatives of a life-saver drug that has improved therapeutic properties," says Manju Sharma, secretary of the Department of Biotechnology, which, along with the Council of Scientific and Industrial Research, has been funding the research.

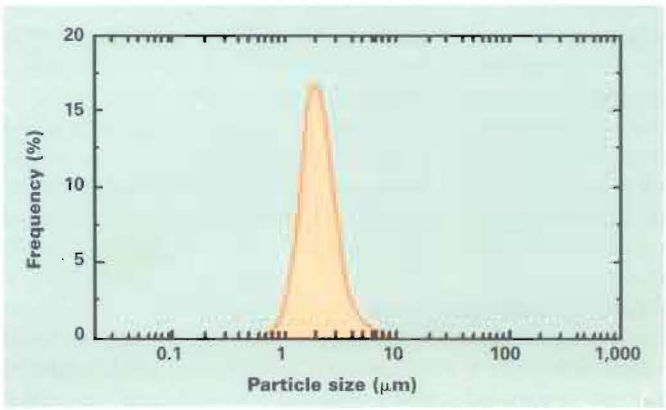
Sahni says that detailed animal model studies and scaling up for production are already underway, with a view to preclinical trials. A commercial tie-up with a pharmaceutical firm would help this endeavour and help to take the technology to the marketplace, he says. Sahni's team includes Rajesh Gupta, K. Rajagopal, Mahavir Yadav, Deepak Nihalani and Chaiti Roy.

1. Chaudhary, A. *et al. Prot. Sci.* 8, 1–15 (1999).

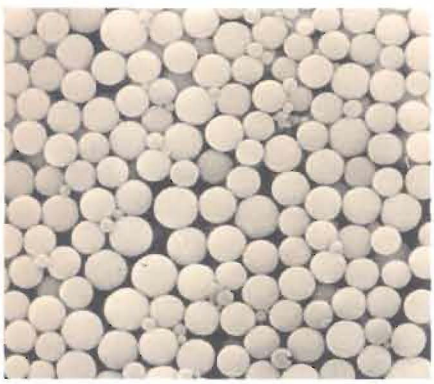
Polyurethane microspheres via new technique

Pune scientists at the National Chemical Laboratory in Pune have obtained a US patent (5859075) for their technique of preparing free-flowing polyurethane particles of uniform size in the range 0.1 to 100 micrometres.

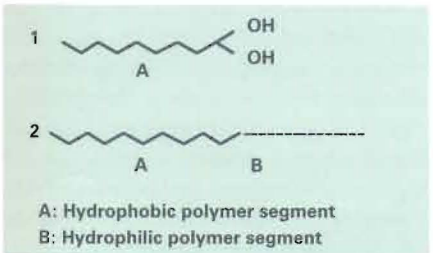
"Such polyurethane powders have potential applications in the field of coatings and paints, as well as carrier materials for encapsulation and controlled release of a variety of active agents," says S. Sivaram, deputy director of the laboratory and one of those behind the process. "Many of these applications need polyurethane particles to be in a monodisperse spherical form" on the order of nanomatres to micrometres across.



The microspheres created are extremely uniform in size, with most being between 1 and 10 micrometres (μm) in diameter.



Microspheres prepared using the new technique.



The process uses a reactive diol with a long hydrophobic moiety (1) and an amphiphilic block co-polymer (2).

Along with P. G. Shukla, Sivaram has demonstrated the feasibility of preparing such particles through the non-aqueous dispersion polymerization of an isocyante with a diol. "The method is general, applicable to wide variety of diols and isocyanates, and is simple," Sivaram told *NewsIndia*. The key to successful particle-forming polymerization is the use of new steric stabilizers, he says, such as a reactive diol containing two primary hydroxyl groups with a long hydrophobic moiety and an amphiphilic block co-polymer.

According to the scientists, this new class of macrodiol steric stabilizer participates in the reaction to form urethane and is enchained in the polymer. The hydrophobic moiety of macrodiol or block co-polymer stabilizes the polyurethane particles formed by the steric stabilization mechanism. How well the macrodiol and the block co-polymer perform as stabilizer depends on the relative molecular weight, co-polymer composition, and concentration. The new process has been shown to be useful for the preparation of microcapsules of water-soluble agents[1].

Conventionally, polyurethane particles are prepared by cryogenic grinding of thermoplastic polyurethanes or by suspension polymerization of isocyanate terminated prepolymers in aqueous or non-aqueous medium. The particle-forming polymerizing processes reported so far are typically performed with vinyl monomers. According to Sivaram, there has been only one report of particle-forming polymerization of isocyanate with a diol to produce polyurethane microspheres. The process developed in Pune is the second to use these ingredients.

1. Shukla, P. G. & Sivaram, S. *Microencapsulation* (in the press).