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## Effect of Different Composition on Particle Size Chitosan-PMAA-PNIPAM Hydrogel

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### Abstract

Chitosan-based (chitosan-poly(methacrylic acid)-poly(N-isopropylacrylamide) [Cs-PMAA-PNIPAM] copolymer hydrogels were synthesized by free radical emulsion polymerization to study the effect of different composition of monomer on hydrogel particle size. Chitosan usually applied for medical use such as drug delivery due to its biodegradability, bio-compatibility, and non-toxicity properties. Co-polymerized chitosan with MAA and NIPAM is an improvement of chitosan gel to be more responsive to the environment of human body included different pH, temperature, ionic strength, electric field, and enzyme activities. Small size of the particles is particularly important to ensure the particles reach the target site especially as a drug delivery. A full factorial experimental design ( $2^3$ ) was employed to identify which factors influenced most on the particle size. The design considered three factors which is amount of MAA, NIPAM and N,N'-Methylenebisacrylamide (MBA) while particle size are chosen as the responses of the variation on each composition. Particle size distribution was measured by laser diffraction in wet condition. From the design of experiment, NIPAM shows the main factor affected the particle size. However combination of the others factors also contributed on the whole size of the hydrogel.

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### 1. Introduction

Chitosan is much known especially in medical and pharmaceutical application. Its biocompatible properties allow

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it usable in medical application such as topical ocular application<sup>1</sup>, implantation<sup>2</sup> or injection<sup>3</sup>. Chitosan also metabolised by certain human enzymes and this considered that chitosan is biodegradable<sup>4</sup> and also bioadhesive due to positive charges at physiological pH which increase retention at the site of application<sup>5</sup>. Others than that chitosan promote wound-healing especially in veterinary medicine<sup>6</sup> and has bacteriostatic effects with broader spectra of activity, a higher killing rate, and lower toxicity toward mammalian cells<sup>7</sup>. Since chitosan properties are excellent in swollen state, therefore chitosan in hydrogel form is selected for medical application and further research on chitosan hydrogel for multi-purpose application will be more advantages<sup>8</sup>.

Its' performance as a drug delivery give more attraction in medical field especially when chitosan become more responsive to the environment in human body. Copolymerized chitosan with MAA and NIPAM is one of alternative to enhance the pH and temperature responsive of the chitosan hydrogel. However, different composition of chitosan, MAA and NIPAM monomer during copolymerization result on different particle size of the hydrogel. Particle size is particularly important on biodistribution and circulation profile within the body<sup>9</sup>. Varied size of hydrogel carrier in body resulting in different blood circulation times. Once hydrogel is injected into circulation system, certain hydrogel usually small particle size below 10 nm will be removed and certain over than 10 nm will be penetrated into small capillaries within the body tissues<sup>10</sup>. Hydrogel with particle size with range from 50 to 500 nm is usually being used with prolong circulation time and suitable for drug delivery which take days and sometimes almost a month in circulation system. Hydrogel with larger than 4  $\mu\text{m}$  which is the smallest diameter size of capillaries system will be captured and withheld in the lung. This will risk on human body<sup>11</sup>. However particle size of hydrogel in different part of human body is depend on its site target and also its application such as particle size of hydrogel for oral delivery can be larger compared to particle size for transdermal or blood by injection.

Since Chitosan-PMAA-PNIPAM hydrogel function as a carrier in body system, it is particular to achieve particle size in range below 500 nm so that the application of this chitosan-PMAA-PNIPAM will be enhanced for any part of body. An experimental design is use to study the main factor affected the particle size and correlation each of the factors that contributed to variation of hydrogel size.

### Nomenclature

CS-PMAA-PNIPAM	Chitosan-poly(methacrylic acid)-poly(N-isopropylacrylamide)
Chitosan	Chitosan
MAA	Methacrylic acid
NIPAM	N-isopropylacrylamide
MBA	N,N'-Methylenebisacrylamide
DDH <sub>2</sub> O	Deionised distilled water

## 2. Experimental

### 2.1. Materials

N-isopropylacrylamide (NIPAM), N,N-Methylenebisacrylamide (MBA) (purity > 95.0%) and Chitosan (Mw  $\approx$  160,000 g/mol, degree of deacetylation  $\approx$  91.0%) were purchased from Aldrich (St. Louis, MO, USA), and all other chemicals were obtained from Acros (Geel, Belgium). NIPAM was purified by recrystallization from toluene/n-hexane (1:3) mixture. Methacrylic acid (MAA) (purity > 95.0%) was further purified through distillation under reduced pressure, whereas all other chemicals were used as received and without further purification. Deionised distilled water (DDH<sub>2</sub>O) was used for all reactions, solution preparations, and hydrogel purified by using membrane filter, which was obtained from a Milli-Q@system, Millipore (Bedford, MA, USA).

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