

# **2003 TAIWAN INTERNATIONAL SCIENCE FAIR**

**CATEGORY : Biochemistry**

**PROJECT TITLE : Synthesis, Characterisation, and  
Temperature-sensitivity of  
Hydroxyl-Terminated  
Poly(N-isopropylamide)**

**AWARD : First Award**

**SCHOOL : Raffles Junior College**

**FINALISTS : Chong Yao Feng Victor**

**COUNTRY : Republic of Singapore**

# Synthesis, Characterisation, and Temperature-Sensitivity of Hydroxyl-Terminated Poly(*N*-isopropylacrylamide): Towards Building Polymeric Micellar Drug Carriers For the Targetable Delivery of Anti-cancer Drugs

Chong Yao Feng Victor

## **Background:**

Delivery of anticancer drugs *in vivo* can be achieved by using target-specific drug carriers of various types – e.g. microspheres and liposomes – which can be applied intravenously, or subcutaneously via a hypodermal patch, etc. as appropriate to the type of drug carrier employed. Recently, interest has surged in the usage of amphiphilic polymeric micelles for this purpose, as they prove superior to other drug carriers in many ways. They have highly-hydrated hydrophilic shells, and hydrophobic cores wherein hydrophobic anticancer drugs such as adriamycin can be encapsulated during transport in the blood. Their main advantages include their smallness of size – enabling them to elude capture by the reticuloendothelial system (RES) – their stability in the bloodstream as shown in their low critical micelle concentration (CMC) values, their passive targeting of tumour sites via the enhanced permeability and retention (EPR) effect, and their ability to integrate an active targeting mechanism, e.g. antibody-antigen recognition, pH-sensitivity, etc.

## **Purpose of the research:**

The feasibility and properties of a polymeric micellar drug carrier integrating a temperature-based active targeting mechanism was investigated. This was done by synthesising the hydrophilic segment of a thermo-responsive amphiphilic micellar copolymer, and subsequently studying it using spectroscopic methods. The hydrophilic segment prepared in this experiment was hydroxyl-terminated poly(*N*-isopropylacrylamide) (HO-PIPAAm).

## **Procedures:**

HO-PIPAAm was synthesised via chain-transfer radical polymerisation of *N*-isopropylacrylamide (IPAAm), using 2-hydroxyethanethiol as a chain-transfer agent, benzoyl peroxide (BPO) as an initiator and dry THF as a solvent. The solution was degassed by bubbling with dry N<sub>2</sub> and then refluxed at under a N<sub>2</sub> atmosphere for 16 hours. Upon completion, the product was precipitated out by the addition of diethyl ether. The product was further purified by re-precipitation from a mixture of dichloromethane

and diethyl ether via a slow liquid-liquid diffusion method. Finally, HO-PIPAAm was characterised by GPC,  $^1\text{H}$  NMR, IR, and by UV-VIS studies. The UV-VIS study determined HO-PIPAAm's lower critical solution temperature (LCST) – the temperature at which transmittance of 500 nm light through an aqueous solution of HO-PIPAAm dropped to 50%, which is thus also the temperature at which HO-PIPAAm precipitates out of solution.

### **Results and Data:**

HO-PIPAAm was synthesised with a yield of 27.6%. Two products with different weight-averaged molecular weights ( $M_w$ ) were obtained, which were found to be 9350 and 1730 by GPC. The polydispersity indexes were 1.45 and 1.02 for the high and low  $M_w$  polymers respectively. The  $^1\text{H}$  NMR and IR spectra confirmed the success of the polymerisation by showing peaks that corroborated with the type of protons and functional groups present in the theoretical structure of HO-PIPAAm. The LCST was determined to be 32.6 °C.

### **Conclusion:**

These results confirm the success and thus the feasibility of synthesising the hydrophilic segment of an amphiphilic micellar copolymer to be used in anticancer drug delivery. The temperature-sensitivity of the hydrophilic segment was also proven via UV-VIS studies and the LCST found to be 32.6 °C.

## 評語

Good and clear synthesis rationale. Temperature sensitivity can be detected.

Further improvement of the Polymer should lead to practical application in the future.