BIOCOMPATIBLE SUPERPARAMAGNETIC NANOSPHERES FOR THE CANCER TREATMENT

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Introduction

A variety of clinical procedures have been developed to the cancer therapy during the last century. The classical cancer treatment includes the total excision of tumor tissue and adjacent tissues in combination with chemotherapy, immunotherapy or radiation treatment. The development of hyperthermia has brought an additional driving force into cancer therapy. In the hyperthermia treatment magnetic particles introduced in the tumors are inductively heated by a magnetic field at moderate temperatures (41-43 °C). The temperatures in excess of 41 °C inactivate the cancer cells preserving the normal cells of the surround tissues. Due to their biocompatible properties, poly(2-hydroxy methylmethacrylate) (PHEMA) microspheres and nanospheres are among the most promising carriers for the superparamagnetic particles. An important part of our laboratory's research is focused on the encapsulation of the $Y_3Fe_{5-x}Al_xO_{12}$ (YIG) magnetic particles by using biocompatible polymers for the hyperthermia treatment. When microencapsulated the magnetic materials are protected from extracellular enzymatic degradation and the cytotoxicity of the YIG due to the Fe presence may be avoided.

Materials e Methods

Poly(2-hydroxyethylmethacrylate) microspheres containing the polycrystalline particles of $Y_3Fe_{5-x}Al_xO_{12}$ (YIG) ($0 \leq x \leq 2$) were prepared by suspension polymerization in a batch reactor using AIBN as initiator and the cross-linker EGDMA. The reaction was performed at 90 °C under a nitrogen atmosphere for 2 h. After reaction, the microspheres were filtered, washed with distilled water followed by acetone, and then dried in a vacuum oven at 50 °C for 48 h. The synthesized microspheres were characterized by X-ray diffraction (XRD), scanning electron microscopy (SEM) and vibrational spectroscopy (FTIR). The Curie temperature (T_C) was determined from the magnetic susceptibility measurements in the temperature range of 5-473 K. The cytotoxicity assay of the PHEMA/YIG was carried out using the Chinese hamster ovary cells culture (ATCC CHO K1) according to the ISO 10993-part 5.

Results and Discussion

Figure 1 shows the derivative curve for the size distribution determined by differential granulometric analyzes and the SEM micrograph for PHEMA/YIG microspheres. An excellent monodispersities (> 80%) was obtained. The XRD analysis reveals that yttrium aluminum iron garnet samples appear as a single phase. The IR spectrum exhibits stretching bands at 660, 600 and 570 cm^{-1}, characteristics to the stretching mode of YIG tetrahedral. SEM YIG study reveals the presence of aggregates of irregular fine particles. The Curie temperatures (T_C) of YIG estimated from the magnetization curves decreased with the aluminum content probably due to the reduction in the number of the main magnetic interaction. Figure 2 shows that the T_C values for the PHEMA microspheres containing YIG in the composition range of $1.5<x<1.8$ were near to room temperature, indicating that the synthesized microspheres are promissory materials for the hyperthermia treatment. In order to evaluate the possible influence of the PHEMA/YIG microspheres on cells, cytoxicity assay was carried out. It was observed that the presence of the microspheres did not affect the cell viability or the culture growth rate.

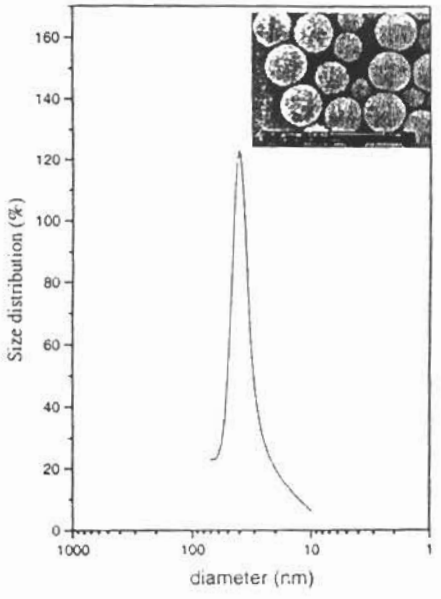

Figure 1- Derivative curve for PHEMA microspheres size distribution and SEM micrograph.

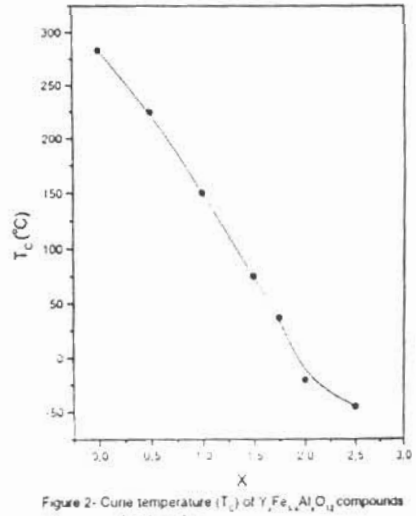

Figure 2- Curie temperature (T_C) of $Y_3Fe_{5-x}Al_xO_{12}$ compounds as function of x.

Conclusion

In according to the results obtained in this work, the synthesized PHEMA/YIG microspheres appears to be promising material for the hyperthermia treatment.