

## *In vivo* study on murine species using Cytarabine magnetic microspheres

Satinder Kakar<sup>1</sup>, Anurekha Jain<sup>2</sup>, Ramandeep Singh<sup>3</sup>

<sup>1,2</sup>Jayoti Vidyapeeth Women University, India

<sup>3</sup>Himachal Institute of Pharmacy, Paonta Sahib, India

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### ABSTRACT

Cytarabine magnetic microspheres were formulated and checked for their antileukemic potential. Leukemia was persuaded in the Wister strain of rat by intravenous injection of benzene. Blood was procured and various hematological parameters were noted and compared. Animals were divided into four groups, antileukemic potential was found to be maximum in case of magnetic microspheres of Cytarabine. The study shows the Antileukemic potential of Cytarabine magnetic microspheres.

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### Corresponding Author:

Satinder kakar,  
Department of Pharmacy,  
Jayoti Vidyapeeth Women University,  
Jaipur, Rajasthan, India.  
Email: satinder.kakkar5@gmail.com

## 1. INTRODUCTION

Magnetic microspheres are the particles that are miniature to circulate through the capillaries but are sufficiently receptive to be encaptured in microvessels by applying magnetic fields of 0.4 T-0.8 T [1]. Success has achieved in dealing with diseases by invention of drugs in histories, which are fulfilling the summons of present day drug therapy i.e. modification of the drug action along with lessening of toxic side effects *in vivo*. Recently a lot of interest has been shown in targeted drug delivery system magnetic microspheres are the one. Targeting i.e. integration of magnetic particles into polymers is covered in MMs. Need for magnetic microspheres: 1) orally administrable pharmaceutical compositions ineffective as a result of absorption of pharmacological active agent in the digestive tract before the target site are reached. 2) Rectal delivery-less convenient and less acceptable than oral formulations. 3) Colon specific drug delivery system-do not delivers the right amount to colon due to RES Clearance. 4) Non magnetic microspheres-cleared off by the RES system. 5) In case of liposomes, resealed erythrocytes the drug carrier suffer major stability problem, hence shelf life is reduced, and so special storage conditions are needed which is not viable. 6) While in Monoclonal Antibodies preparation, selection and isolation of an appropriate antigen for developing monoclonal antibody is again a brain taxing problem, show bad site specificity and are quickly cleared off by Reticuloendothelial system.

However magnetic microspheres show good site specificity and RES Clearance is also minimized. In order to prove any work animal activity is performed thus *in vivo* study of Cytarabine has been performed. Various data reported have shown that benzene is a slow acting poison. It affects the bone marrow part a lot.

The peril of benzene is joined with cumulative exposures of benzene [2]. As Cytarabine is a proved drug for leukemia, therefore it was induced to treat leukemia induced in mice [3-5]. Antileukemic activity of Cytarabine magnetic microspheres is the basic aim for the study.

## 2. RESEARCH METHOD

Cytarabine was procured from Avanscure Lifesciences Pvt Ltd and magnetic microspheres were formulated for it using continuous solvent evaporation method. In order to check the activity of these prepared formulations *in vivo* study was performed on wistar rats. Wistar strain of rats was used for the study. The protocol for performing experiment was approved by Institutional Animal Ethical Committee as per the rules of CPCSEA, India.

Animals were euthanized after accomplishment of the study and the carcasses were disposed as per the guidelines of the institute. Leukemia was persuaded in Wister rats by intravenous administration of 0.2 ml of a 1:10 diluted benzene solution (chloroform in water/2-propanol [50/50] v/v), given each 2 days for 3 weeks successively [5]. Cytarabine magnetic microspheres were administered prior to, during, and ensuing leukemia creation. Leukemia burden was noted by comparing the hematological parameters at baseline and after leukemia induction in various experimental groups. Succeeding 3 weeks of benzene injection, rats in the different groups were bled by cardiac puncture. The blood was collected into EDTA vials, mixed, labeled, and checked [6, 7]. Samples were analyzed for packed cell volume, WBCs, RBCs, hemoglobin, platelets, lymphocytes, RBC distribution width, and mean platelet volume [8-10].

## 3. RESULTS AND DISCUSSION

The results obtained from the study are summarized in Table 1. Significant increase in the parameters such as RBCs, hemoglobin, WBCs and platelets was seen on administration of Cytarabine magnetic microspheres, as the target site specificity is enhanced with the magnetic formulations. Also Reticuloendothelial clearance can be minimized. Thus these formulations show leukemogenic effects.

Table 1. Hematological parameters at baseline, postleukemia induction, and after treatment with treatment with Cytarabine magnetic microspheres

Groups	Sample	Red blood cells	Hemoglobin	White blood cells	Platelets
Normal Control	Baseline	8.68±0.93	15.61±0.65	10.52±0.49	268.37±18.25
	Postanalytical	8.91±0.06	15.82±0.55	10.95±0.06	291.30±18.60
Leukemia Control	Baseline	8.29±0.14	15.40±0.86	11.77±0.30	241.96±18.05
	Postanalytical	5.18±0.02	12.65±0.18*	17.04±0.11	254.49±18.55
Cytarabine magnetic microspheres (50 mg/kg)	Baseline	9.04±0.51	14.88±0.47	10.05±0.82	295.29±19.66
	Postanalytical	8.87±0.61***	14.58±0.37	9.38±0.31*	386.47±26.71**
Cytarabine	Baseline	8.38±0.29	14.78±0.01	10.06±0.19	273.41±19.43
	Postanalytical	7.01±0.82*	13.67±0.97**	10.56±0.74**	251.37±18.20

Results are given as mean±SEM(n=6). Normal control group contrasted with rest of the treated groups with the significance at \* $P<0.05$ , \*\* $P<0.01$ , \*\*\* $P<0.001$ . In time to come by merging different additional policies, microspheres will have chief position in new drug delivery, especially in diseased cell finding, targeted and effective *in vivo* delivery and promoters as mini models of diseased organ and tissues [11-13]. Magnetic Microsphere gives huge chances for formulating new controlled and delayed release formulations, thus extending the borderline of upcoming pharmaceuticals [14-16]. This dosage form provides numerous advantages such as shielding and masking, reduced dissolution rate, easing and handling; spatial targeting of the drug. This system helps in precise delivery of less quantities of potent drugs, diminished drug concentrations at sites other than the target tissue; and protection of unbalanced compounds before and after administration and prior to appearance at the site of action. A research was presented by Gerald G Enriquez, 2013 capable of efficiently delivering sulforaphane, a histone deacetylase inhibitor, for an extended period of time *in vivo*, similarly effect can be obtained for leukemia thus Cytarabine magnetic microspheres are formulated [17]. Magnetic Microsphere technique will discover the important place in new drug delivery system. Especially these can be used for bed ridden patients [18]. Solely, the magnetic microsphere carrier will be broadly utilized in the biomedical field as a beneficial drug carrier [19, 20]. Contrasting with traditional systems; biomass-based drug delivery systems shows higher-ranking drug safety due to their very little pharmacological effects with the matrix [21-24]. Magnetism seems to be a common function of opening a new vista of a multi-barrier of multi-step drug delivery. Their benefit is the

targeting of drug using an external magnet, which can be done very easily. They are relatively novel drug delivery systems, having received attention from the early 1990s. In the early days of twentieth century, Paul Ehrlich envisioned his magic bullet concept-the idea that drugs reach the right site in the body, at the right time, at right concentration [25].

#### 4. CONCLUSION

Benzene is a solvent that is shown to cause leukemia as reported in vast literature studies. Leukemia most commonly it affects the white blood cells. If a person is having problem with the production of RBCs then he may carry leukemia as a disease in future, although there are oral dosage forms, non magnetic microspheres but they are ineffective in targeting the drug to the target site; also they are cleared by the Reticuloendothelial clearance. Thus site specificity is decreased; in order to overcome the magnetic forms were prepared to increase the target site specificity and to minimize RES clearance. Thus there are many future prospects for magnetic microspheres as cancer is the leading disease now a days, it has increased the mortality rate.

Cytarabine is poorly absorbed from the GIT; it shows very good solubility in water. The half life elimination varies in patients depending on the age and it varies from 1-3 hours. As the bioavailability of orally administered Cytarabine is very low thus novel delivery system that is magnetic microspheres have been formulated. In each delivery system therapeutic amount of drug is needed at the needed site. Targeting is drug delivery to the chosen body part to which one wants to deliver the drug. The wanted drug distribution by targeted delivery would leave the rest of the body and thus lowers the overall toxicity while maintaining its therapeutic benefits. Many clinical schemes need delivery of agents that are therapeutic at the desired delivery point. An attempt was made to prepare Cytarabine magnetic microspheres in order to investigate targeting efficiency, enhance bioavailability, and reduce dose and thereby improving patient compliance. Targeting by means of magnetic fields seems to be a vital and most common function of opening a new vista of a multi-barrier of multi-step drug delivery. Their main advantage is the targeting of drug using an external magnet, which can be accomplished very easily thus Reticuloendothelial clearance can be minimized and target site specificity can be increased. Magnetic microspheres are novel drug delivery systems, having received attention from the early 1990s. Thus magnetic microspheres have the great potential for these objectives. This is an effective tool for the cancer patients. The future holds agreement in magnetic microspheres and by supplemental study this will be developed as novel and efficient approach for targeted drug delivery system.

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