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

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| **Article Info** |  | **ABSTRACT** (10 PT) |
| ***Article history:***  Received Jun 12, 201x  Revised Aug 20, 201x  Accepted Aug 26, 201x |  | **Objectives:** Cytarabine magnetic microspheres were formulated and checked for their antileukemic potential**. Material and methods:** Leukemia was persuaded in the wistar strain of rat by intravenous injection of benzene. Blood was procured and various hematological parameters were noted and compared. **Results**: Animals were divided into four groups, antileukemial potential was found to be maximum in case of magnetic microspheres of Cytarabine. **Conclusion**: The study shows the Antileukemic potential of Cytarabine magnetic microspheres. |
| ***Keywords:***  Cytarabine,  Magnetic,  Microspheres,  Leukemia,  Target,  Potential,  Leukemia. |
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1. **INTRODUCTION (10 PT)**

Magnetic microspheres are the supramolecular particles that are small enough to circulate through the capillaries but are sufficiently susceptible 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. incorporation of magnetic particles into polymers are covered in MMs.

**Need for magnetic microspheres**

1. Orally administrable p’ceutical 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 poor site specificity and are rapidly cleared off by Reticuloendothelial system under normal circumstances.

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 Cytrabine has been performed.

Various datas 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 microsphere is the basic aim for the study.

2. **MATERIAL AND METHODS**

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 injection of 0.2 ml of a 1:10 diluted benzene solution (chloroform in water/2‑propanol [50/50] v/v), given every 2 days for 3 weeks successively [5].The Cytarabine magnetic microspheres were administered before, during, and after leukemia induction. Leukemia burden was noted by comparing the hematological parameters at baseline and after leukemia induction in various experimental groups. After 3 weeks of benzene injection, rats in the different groups were bled by cardiac puncture. The blood was collected into EDTA vials, gently mixed, labeled, and checked [6,7].

Samples were analyzed for packed cell volume, white blood cell, red blood cells, hemoglobin, platelets, lymphocytes, RBC distribution width, and mean platelet volume[8-10]

**3.RESULTS**

The results obtained from the study are summarized in table 1.Significant increase in the parameters such as Red blood cells, hemoglobin, white blood cells 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  Postanalytical | 8.68±0.93  8.91±0.06 | 15.61±0.65  15.82±0.55 | 10.52±0.49  10.95±0.06 | 268.37±18.25  291.30±18.60 |
| **Leukemia Control** | Baseline  Postanalytical | 8.29±0.14  5.18±0.02 | 15.40±0.86  12.65±0.18\* | 11.77±0.30  17.04±0.11 | 241.96±18.05  254.49±18.55 |
| **Cytarabine magnetic microspheres (50 mg/kg)** | Baseline  Postanalytical | 9.04±0.51  8.87±0.61\*\*\* | 14.88±0.47  14.58±0.37 | 10.05±0.82  9.38±0.31\* | 295.29±19.66  386.47±26.71\*\* |
| **Cytarabine** | Baseline  Postanalytical | 8.38±0.29  7.01±0.82\* | 14.78±0.01  13.67±0.97\*\* | 10.06±0.19  10.56±0.74\*\* | 273.41±19.43  251.37±18.20 |

Results are given as mean±SEM(n=6). Normal control group compared with rest of the treated groups. Significance at \**P*<0.05; \*\**P*<0.01; \*\*\**P*<0.001.

**4.CONCLUSION**

Benzene is a solvent that is shown to cause leukemia as reported in vast literature studies. Also leukemia is a cancer of the blood or bone marrow. 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[11-13].

Thus there are many future prospects for magnetic microspheres as cancer is the leading disease now a days, it has increased the mortality rate[14-16].

**5.DISCUSSION**

In time to come by merging different additional strategies, microspheres will have the chief position in novel drug delivery, especially in diseased cell sorting, diagnostics, gene & genetic materials, safe, targeted and effective *in vivo* delivery and booster as mini versions of diseased organ and tissues of the body.

Magnetic Microsphere give huge chances for formulating new controlled and delayed release formulations, thus extending the frontier of future pharmaceutical development. These dosage forms provides numerous opportunities such as protection and masking, reduced dissolution rate, easing and handling; spatial targeting of the drug. This system helps in accurate delivery of less quantities of potent drugs; reduced drug concentrations at sites other than the target tissue; and protection of labile compounds before and after administration and prior to appearance at the site of action. In future by combining various other approaches, Magnetic Microsphere technique will find the important place in novel drug delivery system. Especially these can be used for bed ridden patients.

A research was presented by Gerald G Enriquez *et al*, 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]

Consequently, the magnetic microsphere carrier will be widely used in the biomedical field as a favourable drug carrier[18]. Compared with traditional drug delivery systems, biomass-based drug delivery systems shows superior drug safety due to their very little pharmacological effects with the matrix[19,20].

**DECLARE OF INTEREST STATEMENT**

We declare that we have no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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