M. S. Ramaiah college of pharmacy, Bangalore, Karnataka, India

Magnetophoresis: an approach to enhance transdermal drug diffusion

S. Narasimha Murthy

Magnetophoresis is a novel approach in enhancing drug delivery across biological barriers. Benzoic acid, a diamagnetic substance, was selected as the drug candidate. The drug diffusion across rat abdominal skin was enhanced due to the influence of the magnetic field. The experiment with alternating on-off-fields in the same diffusion set-up confirmed that the difference in flux between passive and magnetic diffusion is not due to any variation in the experimental condition or membrane properties. The influence of magnetic field strength on diffusion flux was determined and was found to increase with increasing applied field strength.

1. Introduction

All substances are known to possess a magnetic property. The magnetic property may be classified into three categories, such as ferromagnetic, paramagnetic and diamagnetic depending on their affinity towards the magnetic field. The ferromagnetic substances show maximum acceptability to the magnetic field lines. The paramagnetic substance takes up a position parallel to the magnetic field and acts as a micromagnet. The affinity exists, though it is less than in the first case [1]. But a diamagnetic substance which is of prime importance in the present research, always repels from the magnetic field, or it moves from a field of higher strength to a region of lower strength [2].
According to Puri [3] diamagnetism is a property which arises from the interaction of the paired electrons with the magnetic field and hence is an inherent property of all matter irrespective of whether it also contains unpaired electrons. But in the case of substances containing unpaired electrons, the paramagnetism predominates and hence overshadows the diamagnetism. Diamagnetism is an induced effect and exists as long as the magnetic field lasts, without leading to permanent molecular changes. The property is independent of the magnetic field strength and temperature.
The magnetic susceptibility ($\varkappa$) is defined as the ratio of the intensity of magnetisation (M) produced in the sample to the applied magnetic field (H).

$$\varkappa = M/H$$

where $\varkappa$ is constant depending on H. The gram susceptibility χ_g is given by

$$\chi_g = \varkappa/\varrho$$

where ϱ is the density of the material and the molar susceptibility is given by $\chi_m = \chi_g \times M$ where M is the molecular weight of the substance. The χ_m for diamagnetic substance is negative, in the range of approx. -1×10^{-6} cgs units. The paramagnetic substances has a positive but a very small value (approx. 10 to 100×10^{-6} cgs units), whereas the ferromagnetic substances has a very high values of χ_m (approx. 10^{-2} to $10^4 \times 10^{-6}$ cgs units).
Therefore an experiment was planned with an assumption that application of magnetic field would exert a force of repulsion on the diamagnetic substance and help in enhanced diffusion across the biological membrane.

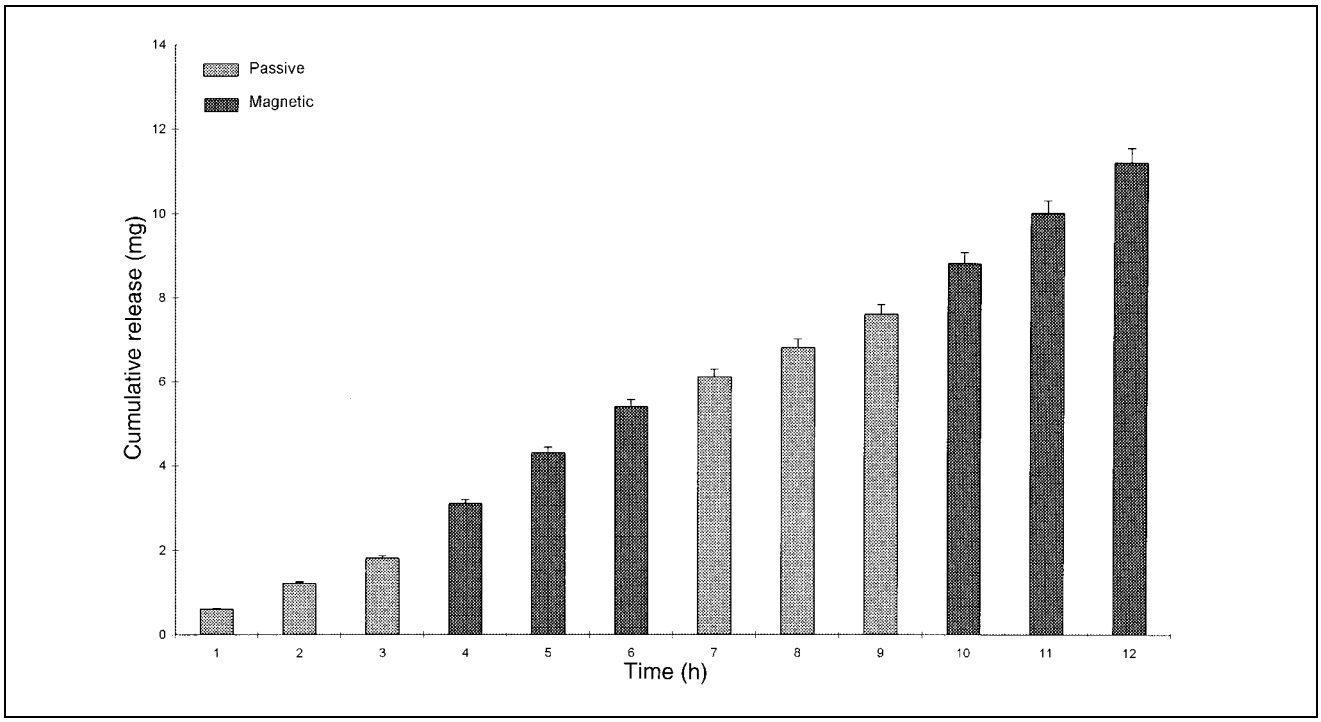

Fig. 1: Passive and magnetic diffusion pattern of benzoic acid

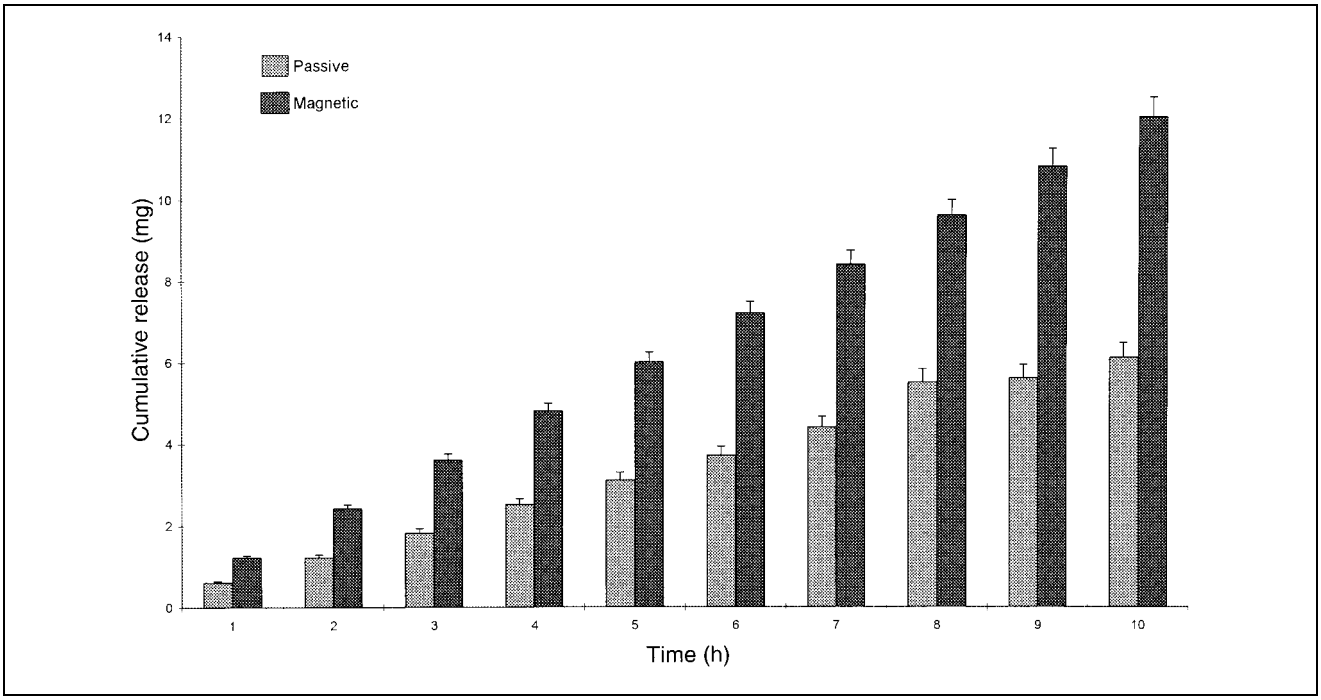

Fig. 2: Diffusion of benzoic acid on alternating on-off magnetic fields

2. Investigations and results

Benzoic acid, whose molar diamagnetic susceptibility value is -70.3×10^{-6} cgs units was selected as the drug candidate [4]. The *in vitro* diffusion studies were carried out in modified Keshary-Chein type diffusion cells across full thickness, untreated abdominal skin of albino rats. Necessary precautions were taken to avoid variation in the experimental parameters. The rate and extent of diffusion was found to be improved significantly in presence of the magnetic field (Fig. 1). Though the results were encouraging in the first set of trials, the possibilities of individual variation in the skin texture could not be ruled out. Therefore the second experiment with the use of the same diffusion cell and the barrier, but alternating with an on-off magnetic field confirmed the true influence of the field on the drug diffusion. The flux was found to be enhanced by the same ratio $\left(\text{flux enhancement factor} = \frac{\text{Magnetic flux}}{\text{Passive flux}}\right)$ when the field was replaced and returned to normal and when the field was absent indicating a clear difference in the passive and magnetically induced diffusion flux. The difference in the diffusion behaviour is evident from Fig. 2. After confirming the magnetophoretic phenomenon, an experiment was undertaken to study the effect of increasing magnetic field on the diffusion flux. The flux enhancement factor increased with increasing field strength (Fig. 3). All the above interpretations were made after six trials and represented in the graphs as average $\pm$SD.

3. Discussion

The reason for the enhanced flux of benzoic acid in presence of a magnetic field can be attributed to the following reasons. Since the diamagnetic substances tend to move out of the magnetic field, they are forced to diffuse across the biological barrier. The possible influence of the magnetic field on the biological barrier leading to some temporary changes in its physicochemical nature favouring the diffusant cannot be ruled out. In addition, the other reason could be magneto-hydrokinesis i.e., facilitated transport of drugs due to osmosis of water under the influence of the applied magnetic field.

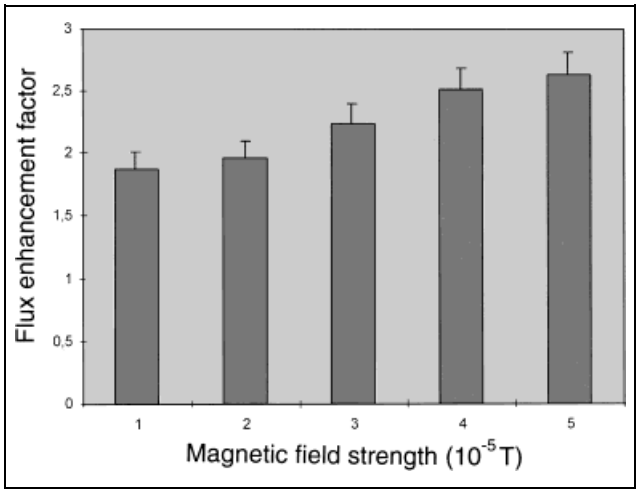

Fig. 3: Effect of increasing magnetic field strength on the diffusion flux of benzoic acid

The results of the experiment give a new hope for the use of magnetic fields as one of the physical means for the enhancement of drug diffusion across physiological membranes in case of topical formulations. The magnetic field is an equally strong field as that of the electric field, which can be used in the same way as iontophoreis leading to a new means of drug delivery as magnetophoresis.

4. Experimental

4.1. In vitro diffusion studies

The *in vitro* diffusion experiment was carried out in modified Keshary Chein type diffusion cells with an arrangement to insert the magnet in the donor compartment. The whole assembly was maintained at a constant temperature of 27 °C. The receptor compartment cell was modified to insert a small mechanical agitator in to the receptor fluid. Freshly excised

abdominal skin of albino rats weighting between 250 to 300 g was cleared of the subcutaneous tissues, without affecting the integrity of the skin layers and used as full thickness skin barriers for the study. The saturated solution (10 ml) of the substance was placed taken in the donor compartment and 50 ml of distilled water was used as the receptor fluid. The cell was applied with a magnetic field by immersing an insulated permanent magnet (magnetic field of 1×10^{-5} T) to 1 cm depth in the donor solution. The receptor medium was agitated at 50 rpm for uniform distribution of the diffused substance. The samples were withdrawn every hour (sink was replaced with the equal volume of distilled water) and the amount of diffused benzoic acid was estimated.
The diffusion studies were carried out in the same apparatus with alternating on-off fields every three hours.

4.2. Influence of field strength

The magnets of different field strength in the range of 1×10^{-5} T to 5×10^{-5} T were used to study the effect of increasing strength on the diffusion of the drug. For a value of magnetic field strength chosen, the experiment was conducted simultaneously in two sets of apparatus, one with and the other without the field, using skin excised from the same albino rat to minimise errors.

The magnetic field does not lead to any kind of degradation of the drug, as could be confirmed by subjecting the drug samples from the donor and receptor compartments to TLC and IR spectroscopy.

References

1 Dutta, R. L.; Syamal, A.: Elements of magnetochemistry, p. 3, East West Publishers, New Delhi 1993
2 Mulay, L. N.; Boudreaux, E. A.: Theory and applications of molecular diamagnetism, vol. 10, Wiley-Interscience, New York 1986
3 Puri, B. R.; Madan, S. P.; Sharma, L. R.: Principles of physical chemistry, p. 1030, Vishal Publications, Jalandhar 1988
4 Rakshit, P. C.: Physical chemistry, p. 324, Web impressions ltd, Calcutta 1988

Received July 3, 1998
Accepted September 28, 1998

S. Narasimha Murthy
Department of Pharmaceutics
M. S. Ramaiah College of Pharmacy
M.S.R.I.T. Post
Bangalore – 560054, Karnataka
India