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Study of drug diffusion rate by laser beam deflection technique

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Abstract. Drug administration is an unavoidable part of treatment. When a drug is administered orally or intravenously, it gets absorbed into the blood stream. The rate and efficiency of absorption depend on the route of administration. When a drug is administered through the oral route, it penetrates the epithelial cells of the intestinal mucosa. The diffusion of the drug into the blood stream depends on various parameters, such as concentration, temperature, and the nature of the mucous membrane. The passive diffusion of drugs is found to obey Fick's law. Water soluble drugs penetrate the cell membrane through aqueous channel or pores. Hence, the study of diffusion of drugs into the water and finally into the blood stream is important. An attempt has been made to study the diffusion of the drug in water as 60% to 80% of human body is water. For the study of drug diffusion in water, a commonly used cough syrup of specific gravity 1.263 is used. It is found that the diffusion rate increases with the concentration of the drug. [DOI: 10.1117/1.JBO.22.6.068001]

Keywords: laser beam deflection; diffusion coefficient; Fick's law; sodium chloride; syrup.

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1 Introduction

With the advent of lasers and data acquisition systems, optical techniques have emerged as potential tools for the measurement of physical properties of matter. Optical techniques are based on certain phenomena, such as refraction, interference, diffraction, polarization, etc.[1] The use of low-power lasers has gained significant attention in the field of science and technology because of its nondestructive nature. It is this property that is being widely used in biomedical characterisations.[2–5] There are several nondestructive optical methods[6–10] for the evaluation of physical parameters, such as drug's diffusion coefficient, tissue's refractive index,[11] and thermal conductivity,[12] etc.

Laser beam deflection (LBD) technique is a nondestructive evaluation method in which the refractive index gradient (RIG) produced in a medium is analyzed for the estimation of physical parameters.[13] Variations in temperature, pressure, concentration, etc. can induce an RIG in a medium. When a beam of light passes through a medium of varying refractive index, it undergoes deflection.[13–16] The refractive index of a liquid medium is found to increase with the concentration of solute particles in it.[17–19] A study of beam deflection due to RIG can give information regarding the physical property of the medium. When one liquid diffuses into another, the refractive index of the medium changes continuously and, hence, the laser beam passing through it gets deflected.

Diffusion is one such phenomenon that depends on the concentration, temperature, viscosity, and density of fluids. This is the basic phenomena of mass transport in biological systems and is governed by Fick's law of diffusion.[20] By Fick's first law of diffusion, the rate of transfer (J) of the diffusing substance through the interface is proportional to the concentration (C) gradient $(\partial C/\partial y)$ measured normal to the interface and is given by

$$J = -D\left(\frac{\partial C}{\partial y}\right). \tag{1}$$

For binary diffusion between two pure fluids, by Fick's second law of diffusion, the rate of change of concentration is proportional to the curvature of the concentration gradient with respect to the distance from the interface and is given by

$$\frac{\partial C}{\partial t} = -D\left(\frac{\partial^2 C}{\partial y^2}\right). \tag{2}$$

The diffusion phenomenon finds applications from the germination of seeds to the administration of the drug. Drug administration is an important problem in estimating the dose of drug required to achieve its adequate concentration in the blood. Drug accumulation in the blood stream depends on drug diffusion rate in the blood. With the development of new drugs and methods of drug delivery into tissues and blood, numerous studies are reported in this field.[21–25]

There are several techniques for the study of diffusion coefficient, such as collimated light transmittance method,[22–25] interferometric method,[26] isotropic methods,[27] etc. All these methods are based on the study of the concentration of the diffusing liquid at a particular spatial point as a function of time. The LBD technique employed in the present study gives information about the diffusion process at various spatial points simultaneously. This can effectively improve the accuracy of the measurement of diffusion coefficient over other conventional techniques. The method also helps in understanding the spatial anisotropy of the liquid medium. In the present work, an attempt has been made to study the variation of diffusion coefficient with concentration, taking sodium chloride (NaCl) as an example. The result of diffusion of NaCl solution into water led to the study of drug diffusion. Drugs and chemicals can also diffuse

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into the blood stream. Human blood consists of 55% plasma in which 92% is water. The diffusion process greatly depends on the density and/or concentration of the diffusing liquid. As the density of water (1.00 g/ml) is close to that of blood plasma (1.025 g/ml), the diffusion of the drug into blood plasma can be studied with water. Hence, the study of diffusion of the drug into water will give information regarding the nature of diffusion of the drug into blood plasma and its spreading into the cardiovascular systems. Phenylephrine hydrochloride and chlorpheniramine maleate syrup is a commonly used drug for common cold, flu, allergies, or other breathing illnesses.[28]

2 Experimental Method

The schematic of the experimental setup for Wiener's method[29] for the determination of diffusion coefficient is shown in Fig. 1. A helium–neon laser with wavelength 632.8 nm and power 2 mW is used as the source. The beam is passed through a cylindrical lens to produce a fan of light. A glass rod of diameter 0.5 cm is used as the cylindrical lens. The fan of light on passing through the homogeneous liquid sample in the cuvette traces a straight line on the screen. The liquid, whose diffusion coefficient is to be determined, is slowly pipetted to the bottom of the cuvette. NaCl solutions of concentrations 0.10, 0.20, 0.24, and 0.30 g/ml were prepared in distilled water at room temperature. These solutions were used for the determination of diffusion coefficient of NaCl solution into water. To study the diffusion of the drug, samples of various concentrations were prepared by adding 0.1, 0.2, 0.3, 0.4, ... ml of drug into 1 ml of distilled water. The experiment is carried out at normal temperature and pressure.

Due to concentration difference between the solvent (water) and the solution, an interface is formed in the cuvette as shown in Fig. 2. The rays emerging from the cylindrical lens on passing through the binary solution get deflected at the interface and produce an image as shown in Fig. 3.

The images of the dip at different time intervals after the formation of the interface are recorded. Let y be the depth of the dip at time t. By noting down the half width at the half maximum $(y_{1/2})$ and at different time intervals (t), a graph is plotted with $(y_{1/2})^2$ versus t as shown in Fig. 4.

A linear fit is given to the plot from which the slope can be calculated. The diffusion coefficient is given by[30,31]

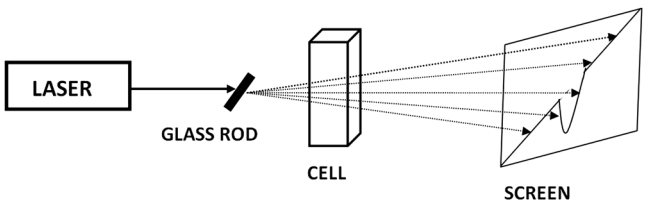

Fig. 1 Schematic diagram of experimental setup.

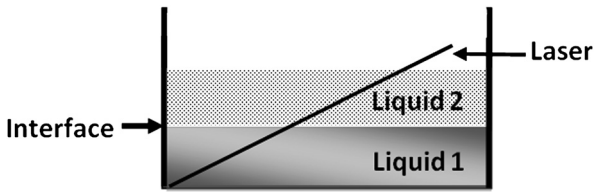

Fig. 2 Formation of interface between liquids in cell.

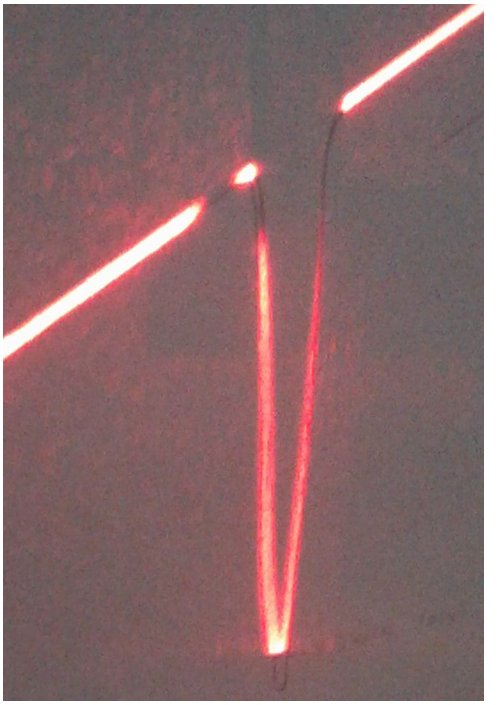

Fig. 3 Image traced on the screen by beam deflected at the interface.

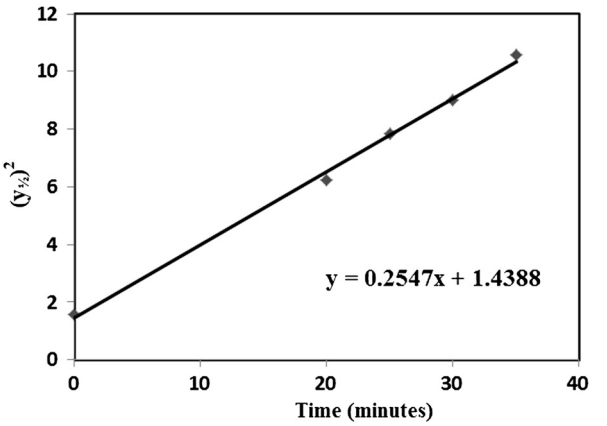

Fig. 4 Plot of $(y_{1/2})^2$ versus t for NaCl concentration 0.1 g/ml.

$$D = \frac{\text{slope of } y_{1/2}^2(t)}{4 \ln 2}. \tag{3}$$

3 Results and Discussion

To study the variation of diffusion coefficient with concentration, NaCl solutions of various concentrations were prepared. Figure 5 shows the variation of diffusion coefficient with concentration.

From Fig. 5, it can be seen that the diffusion coefficient increases with concentration. The graph is in agreement with the polynomial relation connecting the diffusion coefficient and concentration given by Eq. (4), where $|D_0| < |D_1|$, and is shown in Fig. 6.

$$D(C) \cong D_0 + D_1\sqrt{C}. \tag{4}$$

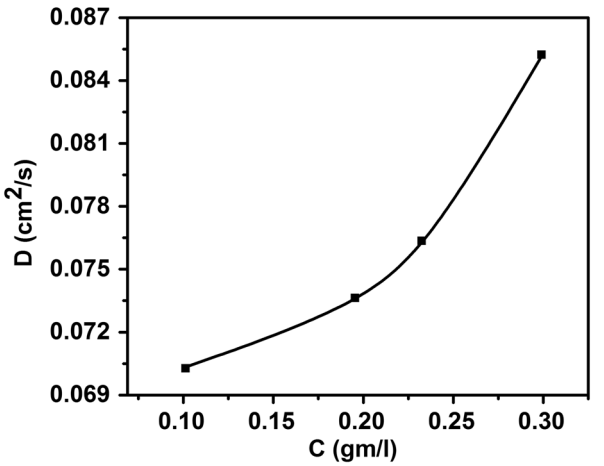

Fig. 5 Variation of diffusion coefficient with concentration for NaCl.

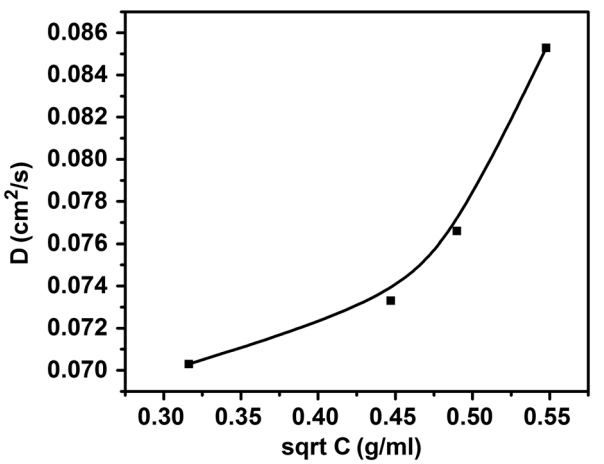

Fig. 6 Variation of diffusion coefficient with square root of concentration of NaCl.

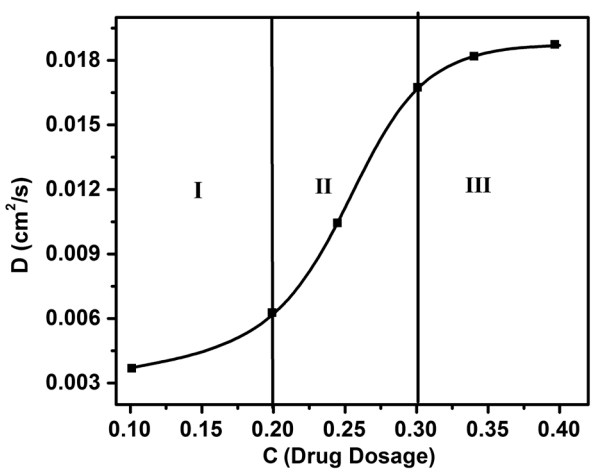

Fig. 7 Variation of diffusion coefficient with the concentration of syrup.

In order to study the diffusion of drugs into blood plasma, a commonly used cough syrup (phenylephrine hydrochloride and chlorpheniramine maleate syrup) was selected. As 92% of plasma is water, the diffusion of the drug into the water can give information regarding the diffusion of the drug into the blood plasma.[32–35] The variation of diffusion coefficient with the concentration of the drug is shown in Fig. 7.

Drug samples of various concentrations were prepared by adding 0.1, 0.2, 0.3, 0.4, ... ml of drug into 1 ml of distilled water. In Fig. 7, we can see three regions of diffusion for concentrations (0 to 0.2, 0.2 to 0.3, and above). In the first region, the diffusion rate increases gradually with the dosage of the drug. In the second region, we can see a sharp increase in the diffusion coefficient with the drug dosage. In this region, a slighter change in the drug dosage produces greater variation on diffusion coefficient. In the third region, we can see saturation of diffusion coefficient with drug dosage. This indicates that the diffusion rate cannot be increased beyond a certain value (0.0187 cm^2/s) of drug dosage level. One has to be cautious while administering drugs with concentrations within region 2 as the effect of the drug will be reflected in a shorter period of time. Hence, an awareness of drug diffusion into plasma is essential while prescribing the drug dosage level.

4 Conclusion

The dynamics of molecular transport at the interface of two miscible liquids can be understood from the study of the diffusion coefficient. Several techniques for the determination of diffusion coefficient study the variations in the concentration of the diffusing liquid at a particular spatial point as a function of time. The present study based on LBD technique is simple and accurate and provides information about the diffusion process at various spatial points simultaneously. This helps in understanding the time evolution of the spatial anisotropy of the medium. This method is employed to study the variation of the diffusion coefficient with the concentration of NaCl solution and extended to understand the diffusion of the drug into water. As densities of blood plasma and water are nearly equal, it is assumed that the study of drug diffusion into water will give information about the diffusion of the drug into blood plasma and its spreading into the cardiovascular system. From this study, it can be seen that the diffusion coefficient increases gradually with the concentration of the drug in the region 1, rapidly in region 2, and saturates in region 3. Therefore, care should be taken while prescribing the drug dosage level within region 2 as the effect of the drug will be reflected in a shorter period of time.

Disclosures

The authors have no relevant financial interests in the paper and no other potential conflicts of interest to disclose.

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