Indian Journal of Science and Technology Vol. 4 No. 6 (June 2011) ISSN: 0974- 6846

Investigation of the concentration goodness for some liquid drugs using light angular scattering

Nafie A. Al-Muslet[1], Rasha I. Yosif[2] and Mubarak M. Ahmed[1]

[1] *Department of laser systems - Institute of laser - Sudan University of Science and Technology, Republic of Sudan - Khartoum, P. O. Box (407)*

[2]*Department of Physics, College of Science and Technology, Omdurman Islamic University, Sudan - Omdurman, P.O. Box 385*

mnmfa2008@yahoo.com

Abstract

In this work a simple setup was built to measure the angular scattering of laser light as an approach for testing the quality of some pharmaceutical solutions (conc.) and detect any change in that concentration with respect to the standard one suitable for desired dose. A laser diode with wavelength 671 nm and output power 100 mW and a photomultiplier tube were used to find the relation between drug concentration and the scattered intensities of the laser beam at angles 45^0, 90^0 and 135^0 with respect to the direction of incidence for the samples: Benzylpenicillin sodium (BS), metronidazole and actrapid HM (insulin human) (IH). The results showed that the relation between the angular scattered intensity and sample concentration is linear. The study proved that this setup is very sensitive to detect the scattered laser intensity for any change in sample concentration from its standard concentration. It was found that even for very small change in the concentration of BS sample, as example by (0.04 g/ml) the setup gave clear reading of this change. Also, a change in the concentration of (IH) sample just by (0.025 g/ml) gave clear differences in the scattered intensity at all angles. From the features mentioned above it is clear that this setup is very efficient in discovering any manipulation in the drug concentration.

Keywords: Laser scattering, goodness investigation, laser industrial applications.

Introduction

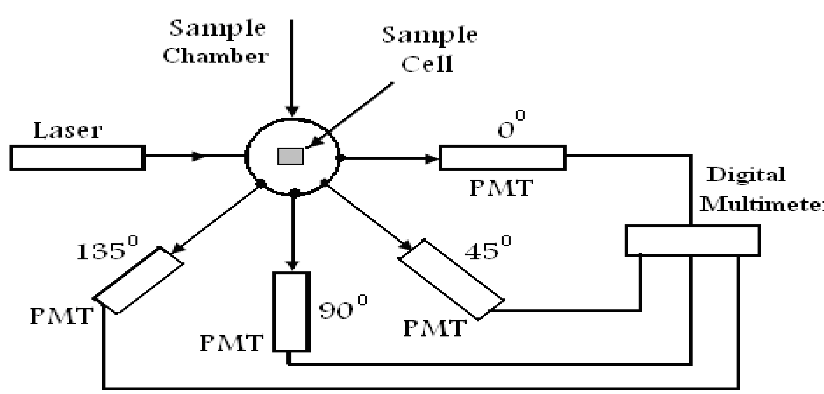
Light scattering is a term referring to physical processes involving the interaction of light and matter. Due to this interaction light incident on an ensemble of particles-crystals, aerosols, molecules, atoms etc. is partially "deflected" in directions deviating from the incident direction. In some scattering processes, in addition to the change in direction, there is also a change in frequency. The evaluation of the scattered light with regard to its intensity and its wavelength often yields valuable information about the scattering matter (Mayinger, 1994; Hahn, 2006). The intensity of the scattered light at different angles (the angular scattering) depends not only on concentration, laser wavelength and particle size but also on the ratio of the refractive indices of the particles to the medium in which the particle exists. The more the particles differ from the medium (i.e. the more their refractive indices differ), the more light will be scattered by the particles. At the other extreme, if there is no difference in refractive indices, no light will be scattered.

The intensity of the scattered light is a function of the wavelength λ, the scattering angle θ, the particle size d and the relative index of refraction n of the particle and the medium. Symbolically, then (Gotterer *et al.,* 1961):

$$I_{sc} = I_{in}(\theta, \lambda, d, n) \quad (1)$$

Limitations and conditions as noted previously are assumed. It should be noted that it was relative to the angle θ at which the incident light was directed. The intensity of light scattering signal recorded at the detector is a function of the scattering power of the particles. The scattering power depends on the particle's scattering cross-section and (in the case of a distribution) the volume (or number) of particles of each size. At low concentrations (single scattering), doubling the concentration of particles of any one size will double the

Fig. 1. The block diagram of the whole system components.



Indian Journal of Science and Technology Vol. 4 No. 6 (June 2011) ISSN: 0974- 6846

scattering contribution made by that size fraction to the total light scattering seen by the detectors (Gotterer *et al.,* 1961).

Measurements of the angular distribution of time-averaged scattered intensity are known as static light scattering (SLS) (Berne & Pecora, 2004), time dependent fluctuations of scattered light intensity due to Brownian motion is dynamic light scattering (DSL) (Schmitz, 1990; Chu, 1991). Static light scattering, normally, deals with the measurements of the angular distribution of time-averaged scattered intensity. This technique can detect changes of the size, shape or structure of the analyzed molecules or particles (Zhelev & Barudov, 2005).

Rayleigh-Debye theory (closely related to Mie theory) was used in this work, because it accounts for the correspondingly more complex angular dependence of the scattering (Chu, 1991).

The experimental part

The angular distribution of the intensity scattered from a number of liquid drugs was measured using a setup constructed by the authors especially for this work. The main units of the experimental setup are: diode laser with wavelength of 671 nm and output power of 100 mW supplied from Rothener company (Germany), specially designed sample chamber with glass cell, photomultiplier tube (PMT), and digital multimeter. Fig. 1 shows the block diagram of the system components. This setup is compact, with low weight and can be used as a portable system.

In this work some liquid drugs were investigated, such as:

Sample 1: Benzylpenicillin sodium (BS):

The chemical structure of benzylpenicillin sodium is 3-dimethyl-7-oxo-6-[(phenylacetyl) amino]-4-thia-1-azabicyclo heptan-

Fig. 2. (Isc/Io) at (45^0, 90^0 & 135^0) as a function of BS

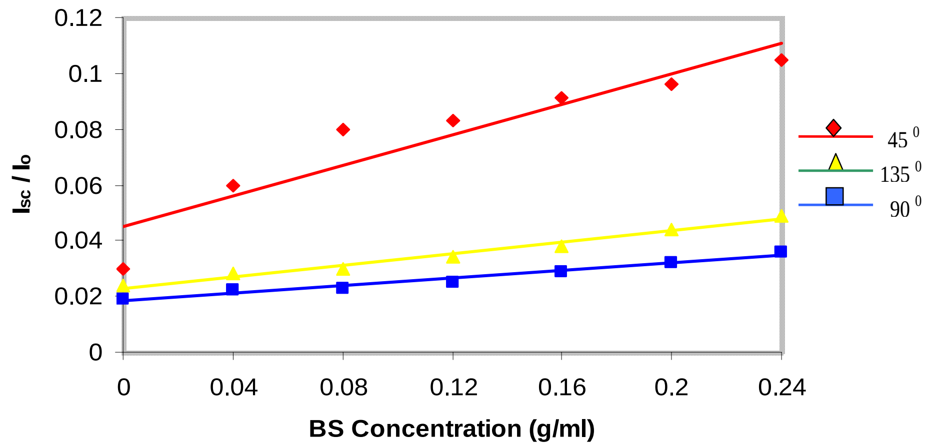


Fig. 3. (Isc/Io) at (45^0, 90^0 & 135^0) as a function of metronidazole conc. ratio.

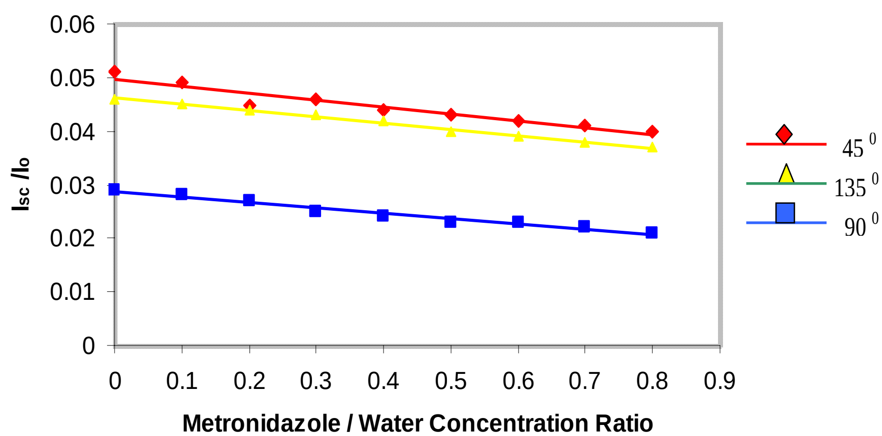
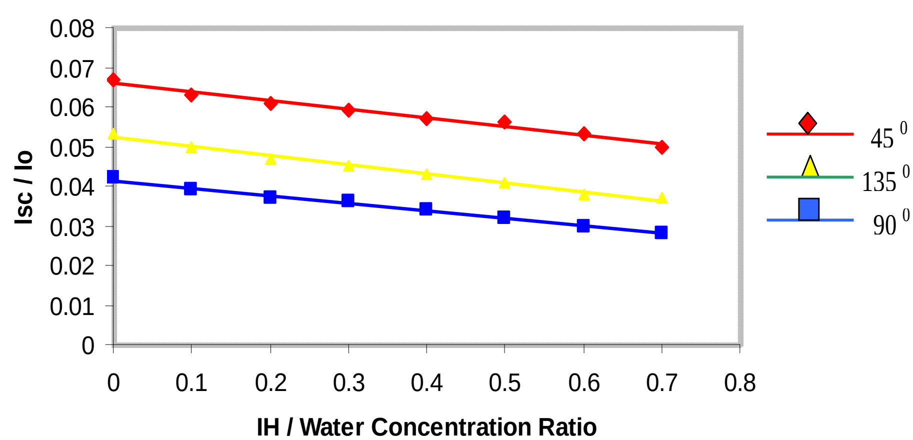
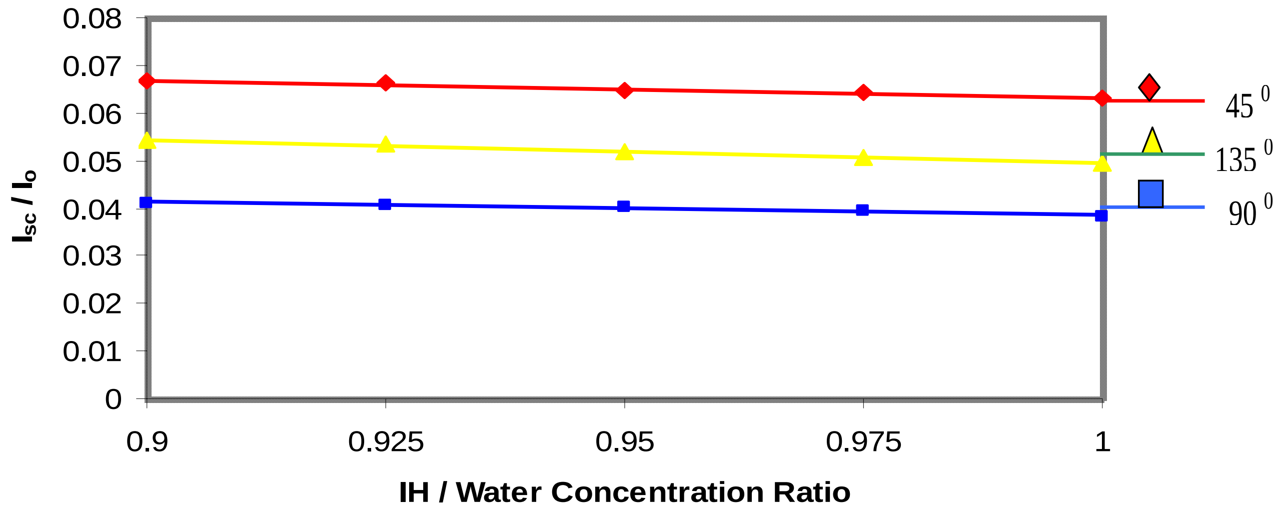


Fig. 4. (Isc/Io) at (45^0, 90^0 & 135^0) as a function of IH with high conc. increment.



Indian Journal of Science and Technology Vol. 4 No. 6 (June 2011) ISSN: 0974- 6846

Fig. 5. (Isc/Io) at (45^0, 90^0 & 135^0) as a function of IH with low conc. increment.



2-carboxylate, a substance produced by the growth of certain strains of *Penicillium notatum* or related organisms, or obtained by any other means (Barton, 1999).

Sample 2: Metronidazole intravenous infusion:

Metronidazole intravenous infusion is a sterile solution of metronidazole in water for injections. The intravenous infusion complies with the requirements stated under parenteral preparations (Barton, 1999).

Sample 3: Actrapid HM (insulin human):

The human insulin is a protein having the structure of the antidiabetic hormone produced by the human pancreas (Barton, 1999).

The concentration of the drug was changed by adding amounts of distilled water to fixed amount of the drug under investigation (dilution).

Results

First of all, the setup was calibrated using known concentrations of dextrose (pure sugar) and pure sodium chloride (salt). The intensity of transmitted and scattered laser light in different angles was measured so that the relation between the scattered intensity, in each angle, and the concentration was checked and compared with the theoretical principles. The results of calibration insured the very good agreement between the theory and the experimental collected data. Then, the scattered laser intensity with angles of 45^0, 90^0 and 135^0 for each sample concentration was measured and plotted.

Fig. 2 shows the variation of the (Isc /Io) as a function of (BS) concentration for the three angles. One can see that (Isc /Io) is increased with the increasing in the concentration for all the angles.

The results obtained from the investigation of scattering via different concentrations of metronidazole are shown in Fig. 3. The same behavior of the (BS) can be noticed for the angles of scattering.

Actrapid HM insulin human (IH) at two different amounts of increment in concentrations were investigated. The results of high concentration increment are shown in Fig. 4, while the results of low concentration increment are shown in Fig. 5.

Discussion

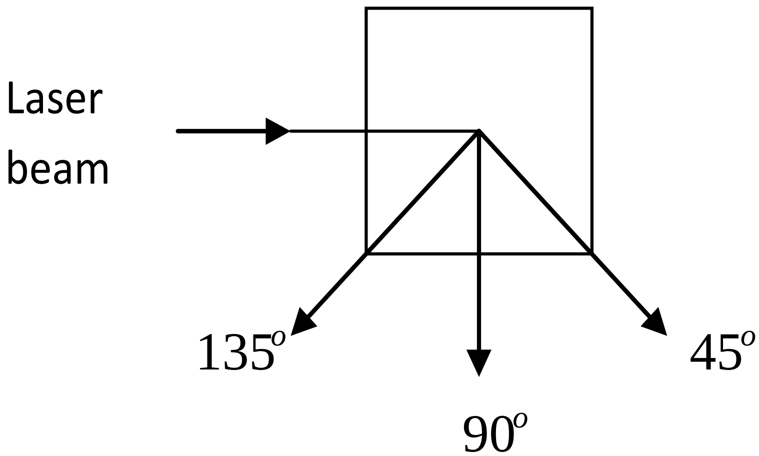
In this work the angular distribution of laser light scattering deduced from a number of pharmaceutical solutions are reported. For all the samples the results gained via scattering at (45^0) showed that the scattered laser light intensity is much higher than those scattered at (90^0) and (135^0), and at the same time the scattered laser light intensity at (135^0) is higher than the scattered light intensity at (90^0).

$$I_{45} > I_{135} > I_{90}$$

This can be explained as follows:
The light scattered at angle of (45^0) has longer path than the others, as shown in Fig. 6, then more collisions in the propagation direction are occurred and the results are more intense scattering. One can see also that (90^0) has shorter path than the others then it produces lowest scattered intensity. The light in the direction of (135^0) has low intensity, and backscattered in the propagation direction increased the intensity than (90^0) but less than (45^0). All samples showed the same behavior for light scattered in different angles. The setup and the detection system are very sensitive for any little change in

Indian Journal of Science and Technology Vol. 4 No. 6 (June 2011) ISSN: 0974- 6846

Fig. 6. The angular distribution of light scattered by (45^0, 90^0 & 135^0).



concentration as can be seen in all figures. All the results of scattering at different angles show considerable decreasing in the scattered intensity with little decreasing in concentration, as example just 0.025. In other words, the setup is very efficient in discovering any manipulation in the drug dose. While available light scattering theory is not sufficiently developed to permit interpretation in detail of the data obtained from particles having the size and geometry of pharmaceutical solutions, we found that the angular distribution of laser light-scattering measurements afford at least two advantages over simple measurements of optical density in the study of pharmaceutical solutions:

(i) The high sensitivity of the measurements of light scattered at angles of 45^0, 90^0 and 135^0 with the incident beam allows studies to be carried out at much lower concentrations of medical solutions than that be feasible by conventional turbidity measurements.

(ii) Measurements of light scattering as a function of angle reflect changes in pharmaceutical solutions size and shape which cannot be detected by optical density studies (Barton, 1999).

For all above reasons the angular distribution of scattered laser light is more accurate technique in concentration investigation. Thus it is a perfect technique for the quality check, from a concentration point of view, where any change in the concentration, due to manipulation or cheating, can be detected via the associated change in the scattered intensity in a very short time.

Conclusion

The graphs of intensity vs. concentration can be used to find the intensity of scattered light that would be expected at some standard concentrations for each particle size. The scattering technique can be used as a mobile technique and it is less expensive compared with other techniques like Spectroscopy as example. Analysis of the scattering intensity as a function of observation angle can lead to particle size distribution. The laser light scattering is fast, uses minimal sample quantities and is not destructive for the sample. In addition, laser light scattering technique does not require special sample preparation.The angular distribution of scattered laser light is a perfect technique of the quality check.

References

1. Barton S (1999) British pharmacopoeia, Stationery office, London. pp: 615-1141.
2. Berne BJ and Pecora R (1999) Dynamic light-scattering. John-Wiley & Sons, NY. pp:376.
3. Chu B (1991) Laser light-scattering, Academic press, NY. pp:1402-1404.
4. Gotterer GS, Thompson E and Lehninger AL (1961) Angular light-scattering studies on isolated mitochondria. *J. Biophy. Biochem. Cytol.* 10(1), 15-21.
5. Hahn DW (2006) Light scattering theory, Academic press, NY. pp: 1-12.
6. Mayinger F (1994) Optical measurements, Springer-Verlag Berlin Heidelberg. pp:16.
7. Schmitz KS (1990) An introduction to dynamic light scattering by macromolecules, Academic press, San Diego. pp:32.
8. Zhelev N and Barudov S (2005) Laser light scattering applications in biotechnology. In: Biotechnology & Biotechnological Equipment. Diagnosis Press, ISSN: 1310-2818. Vol. 19, No:3.