EFFECTS OF X-RAY IRRADIATION ON BLOOD VISCOSITY AND BLOOD COMPONENTS

A.M. ELHAJ[#], A.M. EL KHATIB**, K.A. MARGHANI*, A.M. GSIEA***, M. MOUSTAFA*****

* Department of Physics, Faculty of Science, University of Tripoli, Libya,
[#]e-mail: ahmedlehaag@yahoo.com
** Department of Physics, Faculty of Science, Alexandria University, Egypt
*** Department of Physics, Faculty of Education, University of Tripoli, Libya
**** Department of Medical Biophysics, Medical Research Institute (MRI),
Alexandria University, Egypt

Abstract. In this work, we accurately modelled the influence of shear rate and radiation on the blood viscosity. Blood samples of 50 albino rats were examined under different doses (0.50–6 Gy) at constant temperature 37 °C. The mechanism of interaction between radiation and blood are not very clear. The influence of X-rays on blood viscosity at different shear rates (52.8–264 s^{-1}) is noticed for all doses. The viscosity reduction is observed for radiation doses greater than 3.50 Gy. This could be explained by the fact that the irradiated red blood cells form chains (i.e., rouleaux) which enable the cells to move through the blood in a more streamlined fashion, thus reducing the blood viscosity. Also, the radiation may increase plasma protein concentration, which reduces the viscosity of the blood. In conclusion, the changes in blood viscosity are altered by radiation and this effect can be used as an indicator in understanding the effects of radiation during the whole-body exposure.

Key words: Blood, X-rays, viscosity, shear rates.

INTRODUCTION

The blood is a concentrated suspension of cellular elements including red blood cells (RBCs or erythrocytes), white blood cells (WBCs or leukocytes) and platelets (thrombocytes). The presence of RBCs, WBCs, plasma proteins, chylomicrons, electrolytes, and water changes the internal frictional forces of the blood and, consequently, affect the blood viscosity [29, 37]. It is very important to mention that its viscosity depends on shear rate to which the blood is subjected [13, 39]. At low shear rate, the blood viscosity significantly increases, whereas, at high shear rate, the blood behaves almost as a Newtonian liquid and its viscosity only slightly drops with increasing shear rate [39]. The predominant cause of increasing viscosity when lowering shear rate is the occurrence of RBC aggregation [3].

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The RBCs in whole blood have been observed to aggregate into characteristic structures [10, 27, 26]. The aggregation process appears to be strongly correlated with the presence of the plasma proteins [11]. Normally, in a healthy body, when shear rate increases, all RBC aggregates are dispersed and RBC deformability becomes an important factor determining blood viscosity [3, 10, 11, 13]. Factors that influence blood viscosity are shear rate, hematocrit, total plasma protein, RBC aggregation, and erythrocyte deformability [4, 19, 30, 36, 38]. Other important determinants of blood viscosity are temperature and concentration of macromolecules in the suspending medium, [3, 13, 31]. It is generally accepted that, at constant hematocrit and temperature, low shear viscosity is primarily determined by RBC aggregation, while at high shear viscosity, it is dependent on RBC deformability [3, 9, 12, 21, 22, 28, 33].

Change in RBC rheological properties is often associated with hematological diseases or disorders and, therefore, the blood viscosity has been used in the past as an indicator in the understanding and treatment of diseases [17]. The dependence of blood viscosity on the shear rate shows that blood behaves as a non-Newtonian fluid at lower shear rates [8, 18, 25].

The study of the effects of radiation on the rheological properties of blood reveals important information about the interaction of radiation with biological cells. This information is useful in the determination of the degree of radiation damage, and can help to find a correlation between the dose and the radiation effects [33]. Also, the determination of the reasons for changes in blood viscosity can be used to find the suitable radioprotectors and the convenient therapy for many cases of radiation exposure. To obtain reliable and consistent information, an appropriate rheological model should be applied [23]. In the literature, there are different empirical/semi-empirical equations describing the viscosity-shear rate dependence [3, 10, 17, 21]. In the present paper, we have chosen two models, namely, the power law (PL) model and the Modified Cross (MC) model to explain the blood flow behavior [9, 28, 37].

MATERIALS AND METHODS

The experiments were carried out with a total of 50 adult albino rats weighing 150 g on average. The rats are divided into two main groups: 6 non-irradiated rats used as a control and 11 subgroups each of 4 rats. They were confined in a rectangular plastic box and exposed to X-rays delivered by a clinical therapeutic linear accelerator facility (6 MV) at the Faculty of Medicine of Alexandria, Egypt. The rats were whole-body exposed to the following doses of irradiation: 0.50, 1.50, 2.00, 2.50, 3.00, 3.50, 4.00, 4.50, 5.00, 5.50 and 6.00 Gy, respectively. All the rats were dissected at 10 days after irradiation. The blood samples were withdrawn

from the left ventricle of the heart using heparinized needles. Whole blood viscosity and shear stress were measured immediately after withdrawal from the heart, to avoid any aggregation or RBC rouleaux formation. The applied shear rate was 52.8 s^{-1} to 264 s^{-1}.

The measurements were carried out at a constant temperature of 37 °C in a low shear rotational viscometer (Model DV-II+Pro Viscometer, BROOKFIELD, USA). Practically, the low shear region can be characterized by the consistency index (low shear viscosity) and flow index. They can be calculated from the power law fit of the range of the flow curve. The relationship between the blood viscosity and the shear rate which is considered to describe a non-Newtonian fluid is given by the power law. In our results, the flow behavior of the blood could be well represented by either the PL model or the MC model. Our data were fitted to the PL model:

$$\eta = k\gamma^{m-1} \tag{1}$$

where η is the dynamic viscosity, γ the shear rate, k is the consistency index (i.e. a measure of the consistency of the fluid). The constant m, (i.e., rheological flow index) is a measure of the degree of non-Newtonian behavior. The rheological flow index values are almost unaffected by the RBC concentration. Different models have been proposed to explain the blood flow viscosity. Our data were also fitted to the MC model to estimate zero shear rate viscosity (η^0) and critical shear stress (τ^0) [7, 15]:

$$\eta = \frac{\eta^0}{1+\left(\gamma\frac{\eta^0}{\tau^0}\right)^{1-n}} \tag{2}$$

where n represents the shear rate sensitivity, $0 < n < 1$.

RESULTS AND DISCUSSION

Blood is a non-Newtonian fluid, its viscosity depending on the shear rate. At low shear rate, its viscosity steeply increases primarily because of RBC aggregate to form rouleaux. At high shear rates blood viscosity converges to a limit partially influenced by RBC deformability. Thus, disaggregation and deformation both contribute to blood viscosity decrease [34, 40].

Two plots (Fig. 1(a, b)) represent the comparison of blood viscosity for non-irradiated and irradiated rats. Both figures show blood viscosity as a function of shear rate (52.8 s^{-1} to 264 s^{-1}) at constant temperature 37 °C for different dose

intervals: (0.50–3.00 Gy) and (3.50–6.00 Gy), respectively. At low shear rates, the viscosity is highly determined by RBC aggregation, then it decreases with increasing shear rates due to RBC deformability [3, 9, 12]. Both figures exhibit separated viscosity curves for non-irradiated and irradiated rat groups. In Fig. 1(a), the curves of blood viscosity for irradiated samples are slightly lower than those of the non-irradiated samples. There are little systematic (consistent) separations between the curves for non-irradiated and irradiated samples. In Fig. 1(b), there is a wide separation between curves of viscosities for non-irradiated and irradiated samples. According to our experimental data, one can suggest that a viscosity reduction may be attributed to the mean corpuscular hemoglobin concentration which decreases significantly with dose, and to damage of the cell membrane [32, 33].

The X-ray irradiation increases the plasma protein concentration, which reduces the viscosity of RBC. The reduction in blood viscosity may be attributed to the radiation-induced decrease of protein levels in the blood [24]. After irradiation, the RBC had been approached together forming contiguous chains. This means that the X-ray irradiation had reduced the adhesion between RBCs. It may cause a mechanical change in the blood because weaker bonds are formed if a hydrogen atom in one molecule is attracted to an atom of nitrogen, oxygen, or fluorine in another molecule [14, 20]. The X-ray irradiation of RBC showed a loss of sodium/ potassium ion balance with entry of sodium ions into the erythrocytes and exit of potassium ions. This phenomenon was due in part to discontinuation of membrane integrity [5]. Radiation-induced changes in the properties of cell membranes result in the loss of ability to regulate electrolyte balance and changes in permeability for RBC [1, 6, 35]. The decrease in blood viscosity might be attributed to changes in protein molecular weight, protein structure, and pH sensitivity [1, 2].

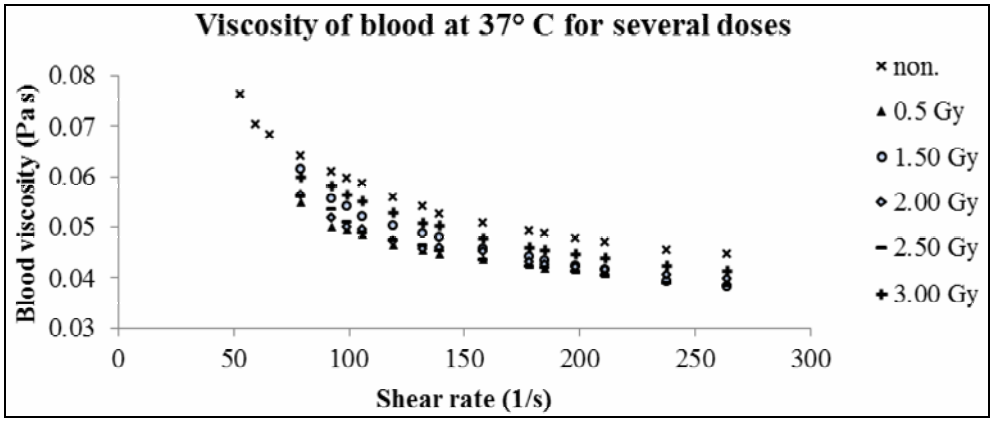

Fig. 1(a). Blood viscosity at 37 °C as a function of the shear rate for different doses: 0.50–3.00 Gy. It shows a small difference between non-irradiated and irradiated rats.

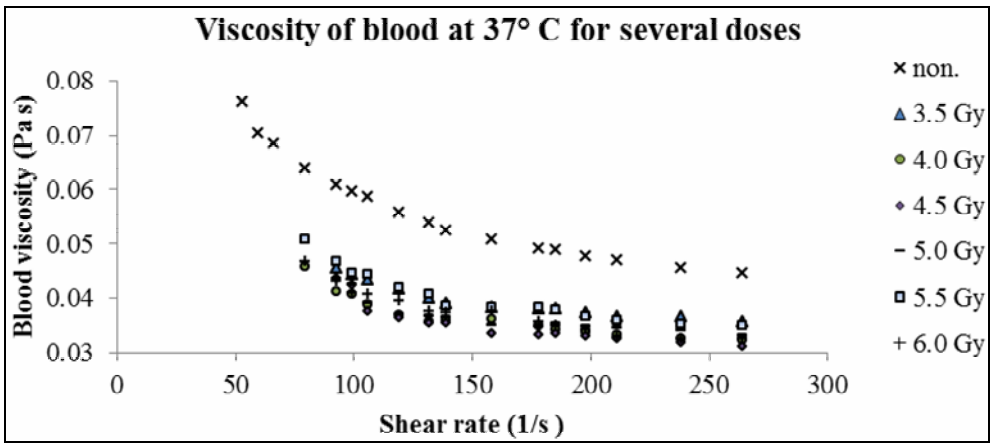

Fig. 1(b). Blood viscosity at 37 °C as a function of shear rate for different doses: 3.50–6.00 Gy. It shows a difference between the curves for non-irradiated and irradiated rats.

In this paper, practically, the low shear region can be characterized by the consistency index (k) and the rheological flow index (m), which can be calculated from the power law fitting of the data of the flow curve. In Table 1, the first column represents several different doses. The 2rd and 3th columns represent consistency index and rheological flow index. The 4th column represents the aggregation index (the ratio of the viscosities in two regions of shear rates: 20 s^{-1} and 100 s^{-1}) that can be regarded as a quantitative characteristic of RBCs [16]. The results of this study indicate that after the RBC exposure to X rays, the viscosities, consistency, and aggregation are decreased as compared with the non-irradiated samples. The value of the flow index remains below unity for the entire dose interval, indicating the non-Newtonian behavior of the blood**.**

Table 1
Power law parameters: consistency index (k), constant flow index (m), and aggregation index (ratio of viscosities at low – 20 s^{-1}, and high – 100 s^{-1} shear rates). Each value represents groups (mean ± SD) for non-irradiated and irradiated rats

Dose (Gy)	k (Pa·s)	m	Aggregation index
0.0	0.28±0.01	0.67±0.01	1.71±0.01
0.50	0.25±0.01	0.67±0.01	1.69±0.01
1.50	0.27±0.01	0.65±0.01	1.75±0.01
2.00	0.18±0.01	0.72±0.02	1.56±.02
2.50	0.22±0.01	0.68±0.01	1.67±0.02
3.00	0.17±0.01	0.74±0.01	1.53±0.02
3.50	0.13±0.01	0.77±0.02	1.45±0.02
4.00	0.14±0.02	0.73±0.02	1.55±0.03
4.50	0.16±0.03;	0.70±0.04	1.62±0.05
5.00	0.12±0.02	0.77±0.03	1.46±0.03
5.50	0.19±0.02	0.69±0.02	1.64±0.03
6.00	0.16±0.01	0.71±0.02	1.61±0.02

To study and monitor the effects of radiation one needs a series of analyses to explore the different damaging events that may occur. In Fig. 2, the blood viscosity at both shear rates, 20 and 100 s^{-1}, as a function of different doses (0.50–6.00 Gy) is presented. The flow curve is characterized by two regions: in the low shear rate (< 100 s^{-1}) and high shear rate (> 100 s^{-1}) up to the shear rate (264 s^{-1}) in which the blood is characterized as a Newtonian fluid. Fig. 2 shows declined curves of blood viscosity as increasing doses due to the effects of X-ray irradiations. This can help to find a correlation between the dose and the radiation effects. The blood viscosity reduction could be explained by the formation of RBC chains due to radiation which enable thus the cells to move through the blood in a more streamlined fashion, reducing the blood viscosity. The irradiation also may increase the protein concentration, which reduces the viscosity.

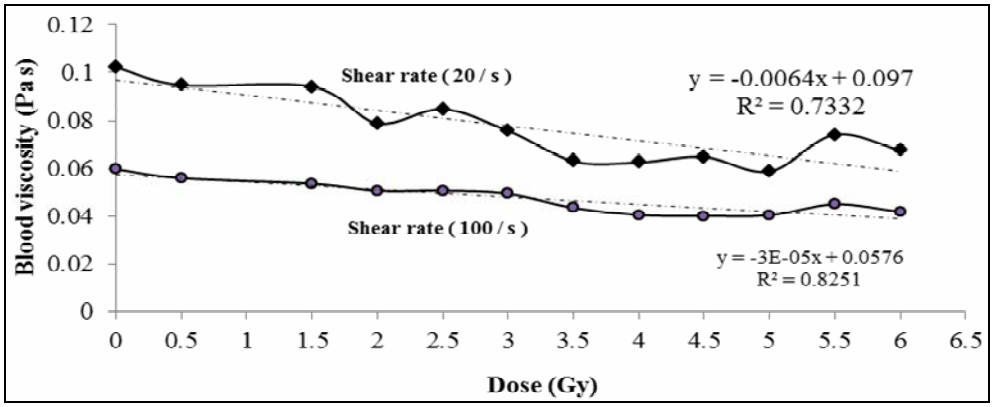

Fig. 2. Blood viscosity at both shear rates (20 s^{-1} and 100 s^{-1}) as a function of different doses (0.50–6.00 Gy). Each point is the mean value from 6 non-irradiated and others each of 4 irradiated rats.

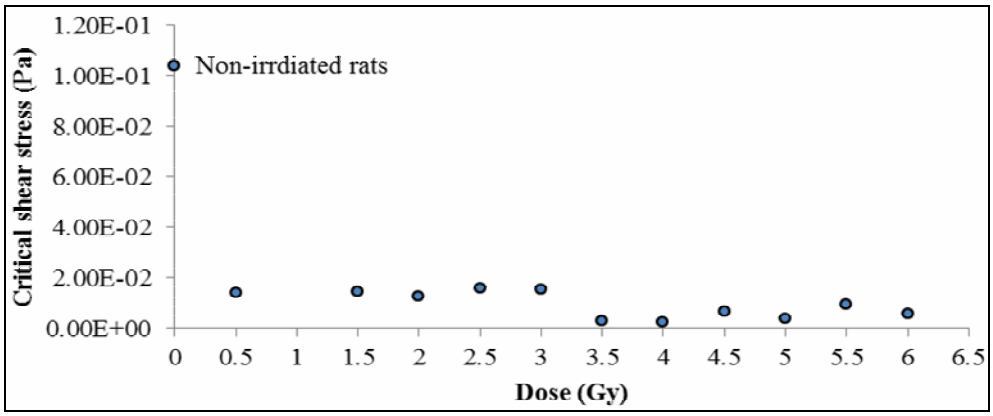

Fig. 3. Critical shear stress as a function of different doses (0.50–6.00 Gy). It shows evident reduction between non-irradiated and irradiated rats**.** Each point is the mean value from 6 non-irradiated and other groups of irradiated rats.

For more analyses, the data of the flow curve are fitted by the MC model to estimate zero shear rate viscosity (η^0) and critical shear stress (τ^0). The critical shear stress calculated from the data fitting as function of different doses is presented in Fig. 3. It shows evident differences between non-irradiated and irradiated rats. It also shows that the level points for irradiated rats are lowered as compared to the non-irradiated ones. This indicates that there is a variability of the rheological properties of irradiated blood samples as function of dose [25].

CONCLUSION

In this report we describe a study of freshly drawn samples of whole blood harvested from rats which were exposed to different radiation doses of X-rays. The flow behavior of blood viscosity was influenced by doses of X radiation. The results indicated that the flow behavior of blood could be well represented by either the power law model or the modified cross model. The reduction of viscosity in irradiated rats indicated a decrease by a similar amount, at low doses (0.50–3.00) Gy, and a gradual drop, at high doses (3.50–6.00) Gy. Both at low and at high doses, the blood viscosity is reduced. The reduction could be explained by RBC chain forming due to radiation. RBC can move through the blood in a more streamlined fashion, thus reducing the blood viscosity. The variability of blood viscosity as function of dose can help to find a correlation between the dose and the radiation effects.

REFERENCES

1. ABABFFI, L., C. HALER, M. TRANDAFIRESCU, D. CERNATESCU, M. IONESCU, Blood changes in calcium and magnesium ion concentrations after whole-body X-irradiation, *Radiat. Res.*, 1970, **42**, 560–564.
2. ABDELHALIM, M.A.K., S.A. MOUSSA, M.S. AL-AYAD, SHORT COMMONICATION Rheological properties of blood serum of rats after irradiation with different gamma-irradiation doses *in vivo*, *Pac. J. Pharm. Sci*., 2016, **29**. 351–355.
3. BASKURT, O., H. MEISELMAN, Cellular determinants of low-shear blood viscosity, *Biorheology*, 1997, **34**, 235–247.
4. BAUM, R.S., Viscous forces in neonatal polycythemia, *J. Pediatr*., 1966, **69**, 975–980.
5. BRESCIANI, F., F. AURICCHIO, C. FIORE, Effect of X-rays on movements of sodium in human erythrocytes, *Radiat. Res*., 1964, **21**, 394–412.
6. BRUGNARA, C., W.H. CHURCHILL, Effect of irradiation on red cell cation content and transport, *Transfusion*, 1992, **32**, 246–248.
7. CARREAU, P.J., Rheological equations from molecular network theories, *Trans. Soe. Rheol.*, 1972, **16**, 99–127.
8. CHARM, S.E., G.S. KURLAND, *Blood Flow and Microcirculation*, John Wiley, New York, 1974.
9. CHIEN, S., S. USAMI, R.J. DELLENBCK, M.I. GREGERSEN, Blood viscosity: Influence of erythrocyte deformation, *Science*, 1967, **157**, 827–829.
10. CHIEN, S., S. USAMI, R.J. DELLENBCK, M.I. GREGERSEN, L.B. NANNINGA, M.M. GUEST, Blood viscosity: Influence of erythrocyte aggregation, *Science*, 1967, **157**, 829–831.

11. CHIEN, S., S. USAMI, R.J. DELLENBCK, M.I. GREGERSEN, Shear-dependent interaction of plasma proteins with erythrocytes in blood rheology, *Am. J. Physiol.* 1970, **219**, 143–153
12. CHIEN, S., S. USAMI, R.J. DELLENBCK, M.I. GREGERSEN, Shear-dependent deformation of erythrocytes in rheology of human blood, *Am. J. Physiol.,* 1970, **219,** 136–142.
13. CHIEN, S., Shear dependence of effective cell volume as a determinant of blood viscosity, *Science*, 1970, **168**, 977–979.
14. COGGLE, J.E., *Biological Effects of Radiation*, Taylor & Francis Ltd., 2nd edition, London 1983.
15. CROSS, M.M., Relation between viscoelasticity and shear-thinning behavior in liquids. *Rheologica Acta*, 1979 **18**, 609–614.
16. DOBROVOL'SKII, N.A., Y.M. LOPUKHIN, A.S. PARFENOV, A. V. PESHKOV, A blood viscosity analyzer, *Biomedical Engineering*, 1997, **31**. 140–143.
17. FEDOSOV, D.A., W. PAN, B. CASWELL, G. GOMPPER, G.E. KARNIADAKIS, Predicting human blood viscosity *in silico*, *PANS*, 2011, **108**, 11772–11777, www.pnas.org/cgi/doi/ 10.1073/pnas.1101210108.
18. FUNG, Y.C., W.C. TSANG, P. PATITUCCI, High-resolution data on the geometry of red blood cells, *Biorheology*, **1**981, **18**, 369–385.
19. HIGGINS, C., Recurrence of venous thromboembolism, *The Biomedical Scientist* (*Magazine*), London, 2006, **50**, 865–867.
20. KENDALL, K., Adhesion: Molecules and mechanics, *Science,* 1994, **263**, 1720–1725.
21. LOWE, G.D.O., J.C. BARBANEL, Plasma and blood viscosity, In: *Clinical Blood Rheology*, G.D.O. Lowe ed., 1988, CRC Press, Inc., Boca Raton, FL, pp. 1–10.
22. MANSUROV, V.A., D.V. MANSUROV, Non-stationary methods of measuring flow curves of law-viscosity settings suspensions*, Journal of Engineering Physics and Thermophysic*s, 2011, **84**, 454–457.
23. MARCINKOWSKA-GAPIRISKA, A., J. GAPINSKI, W. ELIKOWSKI, F. JAROSZYK, L. KUBISZ, Comparison of three rheological models of shear flow behavior studied on blood samples from post-infarction patients, *Med. Biol. Eng. Comput.*, 2007, **45**, 837–844.
24. MEISELMAN, H.J., B. NEU, M.W. RAMPLING, O.K. BASKURT, RBC aggregation: laboratory data and models, *Indian J. Exp. Biol.*, 2007, **45**, 9–17.
25. MERILL, E.W., Rheology of blood. *Physiological Review*, 1969, **49**, 863–888.
26. MERRILL, E.W., E.R. GILLILAND, T.S. LEE, E.W. SALZMAN, Blood rheology: Effect of fibrinogen deduced by addition, *Circ. Res.*, 1966, **18**, 437–446.
27. MERRILL, E.W., E.R. GILLILAND, G. COKELET, H. SHIN, A. BRITTEN, R.E. WELLS, Rheology of human blood near and at zero flow, *Biophys. J.*, 1963, **3**, 199–213.
28. MURATA, T., Theory of non-Newtonian viscosity of red blood cell suspension: effect of red cell deformation, *Biorheology*, 1983, **20**, 471–483.
29. NWOSE, E.U., Whole blood viscosity assessment issues I: Extrapolation chart and reference values, *North Am. J. Med. Sci*., 2010, **2**, 165–169.
30. RAND, P.W., E. LACOMBE, H.E. HUNT, W.H. AUSTIN, Viscosity of normal human blood under normothermic and hypothermic conditions, *J. Appl. Physiol.* 1964, **19**, 117–122.
31. RAND, P.W., W.H. AUSTIN, E. LACOMBE, N. PARKER, pH and blood viscosity, *J. Appl. Physiol*., 1968, **25,** 550–559.
32. SELIM, N.S., O.S. DESOUKY, S.M. ALI, I.H. IBRAHIM, H.A. ASHRY, Effect of gamma radiation on some biophysical properties of red blood cell membrane, *Romanian J. Biophys*., 2009, **19**, 171–185.
33. SELIM, N.S., O.S. DESOUKY, S.M. El-MARAKBY, I.H. IBRAHIM, H.A. ASHRY, Rheological properties of blood after whole body gamma-irradiation, *Iran. J. Radiat. Res*., 2009, **7**, 11–17.
34. SEVICK, E.M., R.K. JAIN, Viscous resistance to blood flow in solid tumors: Effect of hematocrit on intratumor blood viscosity, *Cancer Research*, 1989, **49**, 3513–3519.
35. SHAPIRO, B., G. KOLLMANN, The nature of the membrane injury in irradiated human erythrocytes, *Radiation Research*, 1968, **34**, 335–346.

36. TAMARIZ, L.J., J.H. YOUNG, J.S. PANKOW, H.C. YEH, M.I. SCHMIDT, B. ASTOR, F.L BRANCATI, Blood viscosity and hematocrit as risk factors for type 2 diabetes mellitus: the atherosclerosis risk in communities (ARIC) study, *Am. J. Epidemiol*, 2008, **168,** 1153–1160.
37. VAN DER ELST, C.W., A.F. MALAN, H.V. DE HEESE, Blood viscosity in modern medicine, *S. Afr. Med. J.*, 1977, **52**, 526–528.
38. WELLS, R.E. JR., E.W. MERRILL, H. GABELNICK, Shear rate dependence of viscosity of blood: Interaction of red cells and plasma proteins, *Trans. Soc. Rheol.*, 1962, **6**, 19–24.
39. WELLS, R.E., E.W. MERRILL, Influence of flow properties of blood upon viscosity-hematocrit relationships, *Journal of clinical investigation*, 1962, **41**, 1591–1598.
40. WINDBERGER, U., A. BARTHOLOVITSCH, R. PLASENZOTTI, K.J. KORAK, G. HEINZE, Whole blood viscosity, plasma viscosity and erythrocyte aggregation in nine mammalian species: reference values and comparison of data, *Experimental Physiology*, 2003, **88,** 431–440.