Scripta Scientifica Medica, vol. 28 (1993), pp 40-44

MEDICO-APPLIED CHARACTERISTICS OF SOME BICOMPONENT POLYMER SYSTEMS. FIRST COMMUNICATION. EVALUATION OF ACUTE TOXICITY

R. Cherkezova, Z. Zlatev*, M. Ilarionova**

*Department of Chemistry and Biochemistry, Medical University, Varna, *National Centre of Hygiene, Medical Ecology and Nutrition, Sofia, and **National Centre of Oncology, Sofia*

The acute toxicity of polymer compositions when introduced perorally in rats and intraperitoneally in mice has been determined. The materials examined are plaster-like. Their production is based on a hydrophilized unsaturated polyester resin. The latter is object of investigations elsewhere and enables the obtaining bicomponent polymer systems in combination with a carbamide-formaldehyde or melamine-formaldehyde resins. Experimental animals are selected and observed prior to and after the introduction of polymer substances during different periods of time according to the kind of investigation. Neither changes in animal appearance and behaviour, nor mortality cases for all doses examined are registered. These results define polymer composites as low-toxic ones (according to the IVth class of chemical compounds) and present the first stage in the course of research aiming at evaluating their safety when applied in both medical and stomatological practices

Key-words: Bicomponent polymer systems, hydrophilized unsaturated polyester, acute oral toxicity, acute intraperitoneal toxicity, toxicity classification

INTRODUCTION

The synthesis of bicomponent polymer systems of mutually changing structures creates opportunity to obtain composites combining the properties of single components and possessing a new complex of properties as well. Usage of such materials depends to a considerable extent on the kind of independent highmolecular derivatives, their interrelation and degree of compatibility (8, 15). Optimal conjunction of these conditions allows to meet some specific requirements typical of certain fields such as medicine and dentistry (10, 16). That is why problem actuality consists not only in elaborating new polymer systems but also in programable changing their properties. Thus the elaborated

Address for correspondence:
R. Cherkezova, Dept. of Chemistry and Biochemistry, Medical University, Varna, 55 Marin Drinov St, BG 9002 Varna, BULGARIA

bicomponent systems including tridimensional macromolecular lattices of single components (7) which can pass from a state of independent polymer mixtures to that of intrapenetrating space networks (12, 13) can be considered in this aspect. Materials obtained by this way are plaster-like but concrete compositions possess high strength properties in combination with low relative mass. There exists a possibility to prepare stable and light manufactured articles based on these materials and to apply them in orthopaedical and stomatological practice (such as prostheses, splints, insoles, positive sample imprints in dental mechanics, etc.). In principle, polymer applications in these fields is a long known fact (1, 9, 11).

The objective of the present work is to determine the acute toxicity of elaborated polymer systems in cases of peroral and intraperitoneal manner of introduction.

MATERIAL AND METHODS

The investigation covers cross-linked polymer systems based on unsaturated polyester resin (UPR), carbamide formaldehyde resin (CFR), and melamine formaldehyde resin (MFR). Introduction of a hydrophilized component, i.e. of a 25 per cent ammonia solution results in the formation of a hydrophilized UPR (HUPR) (7, 12) which in this changed state forms together with both water soluble CFR and MFR cross-linked polymer systems, i.e. HUPR/CFR and HUPR/MFR, respectively.

HUPR cross-linking is realized by radical co-polymerization with stirol as a monomer, with cyclohexan peroxide as an initializer, and with cobalt naphthenate as an accelerator. Both CFR and MFR present polycondensation derivatives of formaldehyde with carbamide and melamine, respectively, which are cross-linked in the presence of the corresponding hardeners such as phosphoric acid and ammonium chloride. There exist data about the toxic properties of the aforementioned individual substances in the literature available (2, 5), however, no data can be found concerning cross-linked systems based on them.

The study is performed in accordance with the requirements of the countries of the European Community (14), of the designs and schemes for toxicological examinations of the CMEA countries (3, 4) for industrial, custom and drug chemical substances as well as of the Bulgarian State Standards (6).

Experimental animals are selected in dependence on the kind of investigation. After a 10-day stay enabling the establishment of their health status and the preparation of experiments the animals are divided into groups of appropriate number in order to be included in the examinations.

These animals are bred under standard vivarium conditions: at temperature of 20-24 ^{o}C, relative air humidity of 65-85 per cent, absence of abnormally high concentrations of both ammonia and carbon dioxide, natural ventilation, and natural feeding with standardized food pressed into tablets.

White rats of Wistar breed of both sexes with body weight of 180-200 g are used to determine the acute oral toxicity. The rats were introduced per straight metal probe with a diameter of 2 mm and length of 10 cm 20 per cent suspensions of corresponding cross-linked resin

components. The animals are observed every hour until 6 o'clock daily for 14 days. They are divided into three groups of 6 white rats each given these substances in doses of 6000 mg/kg, 8000 mg/kg, and 10000 mg/kg, respectively.

The acute intraperitoneal toxicity is assessed in BDF hybrid male mice (C 57 B1/6 and DBA/2) with body weight between 19.0 and 24.0 g. The corresponding animals are divided into groups of 10 mice each. The doses of substances applied are based on the results from the performed approximal toxicity and amount as follows: 592 mg/kg, 888.8 mg/kg, 1333.3 mg/kg, 2000 mg/kg, 2500 mg/kg, and 3000 mg/kg.

Polymer systems described above are introduced in the form of suspension in physiological saline. The suspensions are prepared by using Twin-80 surface active agent. Correction of pH of suspensions within physiological limits is carried out by means of sodium bicarbonate in a 7.5 per cent solution of Frow Laboratories firm, UK.

RESULTS

During these terms of observation of the animals no changes of their appearance and behaviour are registered at all. No mortality cases among these animals are established when all the doses applied are concerned. These results do not allow to determine the quantitative parameters of the acute toxicity in cases of both oral and intraperitoneal introductions of the substances. LD_0 is higher than 10000 mg/kg when rats are perorally given cross-linked HUPR, HUPR/CFR, and HUPR/MFR. According to the classification of the toxicity of chemical compounds (BSS 15049-80), these substances presenting a hydrophilized unsaturated polyester or systems based on it can relate according to LD_0 for rat orally to the IV^{th} class of chemical substances - i.e. weakly toxic and weakly dangerous. Concerning the intraperitoneal manner of introduction of polymer products in mice LD_0 is as follows: for UPR and CFR - higher than 3000 mg/kg; for HUPR and HUPR/CFR system = 70/30 mass per cent system - higher than 2500 mg/kg, and for MFR and HUPR/MFR polymer bicomponent system = 60/40 - higher than 2000 mg/kg which allows us to relate them to the low toxic and weakly dangerous chemical substances, too.

DISCUSSION

The insignificant toxicity of these polymer materials can be explained by the optimal structure in the course of combined running co-polymerization and polycondensation processes. It means that monomers are maximally incorporated in macromolecular chains forming space lattices. It results in a minimization of the amount of low-molecular and oligomeric derivatives remaining chemically unlinked into space polymer networks.

CONCLUSION

The examined bicomponent polymer systems based on HUPR, HUPR/CFR, and HUPR/MFR can be considered low toxic and weakly dangerous substances according to the parameter of acute oral and intraperitoneal toxicity.

REFERENCES

1. Волков, М. В., И. А. Мовшович. Применение полимерных материалов в травматологии и ортопедии. Москва, 1972.- 2. Лазарев, Н. В. Вредные вещества в промышлености. Ленинград, 1969.- 3. СЭВ. *Пробл. пром. токсикол.*, 1986, № 2, 33-44.- 4. СЭВ. В: Методические рекомендации по токсикометрии. Москва, 1987, 21-30.- 5. Филов, В. А. Вредные химические вещества. Ленинград, Химия, 1990.- 6. Хигиенна токсикология. Методично ръководство. Под ред. Ф. Калоянова. София, Медицина и физкултура, 1985.- 7. Черкезова, Р. Ц. *Высокомолек. соед.*, сер. Б, **34**, 1992, № 8, 75-77.- 8. Chartoff, R. P., J. Cho, P. S. Carlin. *Polym. Eng. Sci.*, **31**, 1991, № 8, 563-566.- 9. Hastings, G. W. *Plast. Eng. News*, **29**, 1983, № 6, 87.- 10. Kicheva, Y., V. Kostov, M. Mateev, D. Vladkova. *Biomaterialien*, **6**, 1992, № 2.- 11. Kimura, H., F. Teraoka. In: Adv. Joint Newer Struct. Mater. Proc. Internat. Conf. Montreal, 23-25.VII.1990. Oxford, etc., 1990, 193-196.- 12. Mateev, M., R. Cerkesova, M. Marincev. *Plaste Kautschuk,* **40**, 1993, № 2, 47-49.- 13. Mateev, M., R. Cerkesova, M. Marincev. *Plaste Kautschuk*, **40**, 1993, № 6, 200-202.- 14. OECD Guidelines for testing of chemicals. Organization of economical cooperation and development. Paris, 1981-1983.- 15. Paul, D. R., S. Newman. Polymer blends. Vol. 2. New York, 1981.- 16. Wood, A. S. *Mod. Plast. Internat.*, **14**, 1984, № 7, 36.

Medizinisch-angewandte Charakteristik einiger bikomponenten Polymersysteme. Erste Mitteilung. Bewertung der akuten Toxizität

R. Tscherkezowa, Z. Zlatew*, M. Ilarionowa**

*Lehrstuhl für Chemie und Biochemie, Medizinische Universität Varna, *Nationales Zentrum für Hygiene, medizinische Ökologie und Ernährung, Sofia, und **Nationales Zentrum für Onkologie, Sofia*

Zusammenfassung: Die akute Toxizität einiger Polymersysteme bei oraler Einführungsweise in Ratten und bei intraperitonealer Einführungsweise in Mäusen wurde bestimmt. Die studierten Materialien waren gipsähnlich und aufgrund eines hydrophilisierten nichtgesättigten Polyesterharzes aufgebaut worden. Das Harz wurde irgendwoanders analysiert und erlaubte die Herstellung von bikomponenten Polymersystemen zusammen mit Karbamidformaldehydharz oder mit Melaminformaldehydharz. Die gebrauchten Versuchstiere wurden ausgewählt und vor und nach der Einführung der Polymerstoffe während verschiedener Zeitabschnitte laut der Art der Untersuchung beobachtet. Es wurden weder irgendwelche Veränderungen im äußeren Aussehen und im Benehmen der Tiere, noch Sterblichkeitsfälle bei allen untersuchten Dosierungen

festgestellt. Diese Ergebnisse gekennzeichneten die Polymerzusammensetzungen als niedrig toxisch (laut der IV. Klasse der chemischen Verbindungen) und stellten die erste Untersuchungsetappe der Einschätzung deren gefahrlosen Anwendung in der medizinischen und zahnärztlichen Praxis dar.

Application médicale des caractéristiques de certains systèmes polymériques à deux composants. Première communication. Evaluation de la toxicité aiguë

R. Tcherkésova, Z. Zlatev*, M. Ilarionova**

*Chaire de chimie et de biochimie, Université de médecine à Varna; *Centre national d'hygiène, d'écologie médicale et de nutrition, Sofia et **Centre national d'oncologie, Sofia*

Résumé: On a déterminé la toxicité aiguë de compositions polymériques introduites per os chez des rats et par voie intra-péritonéale chez des souris. Les matériaux étudiés sont semblables au plâtre. Ils sont basés sur la résine polyester insaturée hydrophilisée. Cette résine de contact est l'objet d'analyses dans les autres études. Elle donne la possibilité d'obtenir des systèmes polymériques à deux composants en combinaison avec les résines urée-formaldéhyde et mélamine-formaldéhyde. Les sujets d'expérience sont selectionnés et observés avant et après l'introduction des substances polymériques selon le type d'étude qui exige des delais différents. On n'a pas enregistré de changements dans l'apparence et la conduite des animaux; on n'a pas relevé aucune mortalité, quelle que fût la dose étudié.Ces résultats révèlent le caractère peu toxique des compositions polymériques (d'après la classe IV des composés chimiques). Ce n'est cependant qu'une première étape des recherches visant l'appréciation de ces compositions en vue de leurs applications inoffensives en médecine et stomatologie.