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EFFECT OF A SYNTHESIS PRODUCT (BY-PRODUCT OF SALICYLIC ACID) IN COMPARISON WITH BASIS STRUCTURAL COMPOUNDS ON SOME PROTEIC METABOLISM PARAMETERS IN RATS

EFECTUL ADMINISTRĂRII UNUI PRODUS DE SINTEZĂ (DERIVAT AL ACIDULUI SALICILIC), COMPARATIV CU COMPONENȚII STRUCTURALI DE BAZĂ, ASUPRA UNOR PARAMETRI AI METABOLISMULUI PROTEIC LA ŞOBOLANI

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The aim of the study was to relieve the effect of synthesis product (by-product of salicylic acid) administration 5-cloro-2hidroxy-azotil-sulfamoil-fenil benzamide (5ClSA-SA) in comparison with basic structural compounds (salicylamide and sulfanilamide) on some parameters of proteic metabolism on rats. The synthesis product 5ClSA-SA is amide of 5 chlorosalycilic acid with sulfanilamide synthesized at The Technical University, Faculty of Industrial Chemistry of Timisoara. The experimental results demonstrate that the synthesis product has determinate a strong significant increase ($p<0.01$) of proteinemia compared to test, over the physiological limits; salicylamide has induces the significant increase ($p<0.05$), and sulfanilamide has induced the significant decrease ($p<0.05$) of total proteins compared to test but in physiological limits. After the administration of the three substances, the albumin and urea values has strong significant decrease ($p<0.01$) compared to test and under the physiological limits. The synthesis product has not determinate significant differences ($p>0.05$) of creatinine compared to test, obtained values being situated in physiological limits, while salicylamide and sulfanilamide have induced strong significant decrease ($p>0.01$), respectively significant ($p>0.05$) compared to test and under physiological limits.

Key words: protein, albumin, urea, creatinine, rat

Introduction

The present paper study the in vivo effect of 5ClSA-SA synthesis product (5ClSA-SA - amide of 5 chlorosalycilic acid with sulfanilamide, product

synthesized at The Technical University, Faculty of Industrial Chemistry of Timisoara .[2,3,6]) over some protein metabolism parameters in comparison with basic structural compounds of this substance in perspective of therapeutically use.

Materials and Methods

The study was done on 35 Wistar white rats, in five groups: 2 test groups C_1 and C_2 and three experimental groups E_1, E_2 and E_3. The synthesis product (5ClSA-SA), salicylamide (SA) and sulfanilamide (SU) was intraperitoneally administrated for 7 consecutive days to the experimental groups as follow: E_1 – 0.44 mg 5ClSA-SA/kg m.c.; E_2 – 0.185 mg SA/kg m.c.; E_3 – 0.23 mg SU/kg m.c.

The 5 ClSA-SA administrated dozes had 1/10 DL_{50} salycilamide constituent, salycilamide was administrated in dose of 1/10 DL_{50} and the sulfanilamide was administrated in dozes equal to the ones contained in 5ClSA-SA administrated dose. To the C_2 group was administrated the same quantities of distilled water (0.3 ml).

Blood was sampling at zero moment from C_1 group, and at 24 h since the seventh administration from E_1, E_2, E_3 and C_2 groups. Was determinate the total protein, albumin, urea and creatinine values with VET SCREEN tester.

Results and Discussions

The results are presented in table 1 and 2.

Table 1

Average values of total protein (g/dL) and albumin (mg/dL) on experimental and test groups

Group	Protein $\bar{x} \pm Sx$	D.S.	Confidence level 95%	Albumin $\bar{x} \pm Sx$	D.S	Confidence level 95%
C_1	7.41 ± 0.08	0.24	0.19	4.01 ± 0.02	0.17	0.12
C_2	7.50 ± 0.10	0.25	0.19	3.99 ± 0.06	0.16	0.12
E_1	8.23 ± 0.14*	0.37	0.19	2.66 ±0.09*	0.24	0.12
E_2	7.79 ± 0.03**	0.09	0.19	2.90 ±0.05*	0.14	0.12
E_3	7.04 ± 0.13*	0.35	0.19	2.71 ±0.05*	0.13	0.12

*$p<0.01$
**$p<0.05$

Proteinemia on E_1 and E_2 groups has strong significant increase ($p<0.01$) and respectively significant ($p<0.05$), (E_1/C_2: + 9.73%; E_2/C_2 :+ 3.89%), and on E_3 group has significant decrease($p<0.05$), (E_3/C_2: - 6.13%) compared to test, in physiological limits on SA and SU groups [8] on administration of with 5ClSA-SA product.

Table 2

Average values of urea (mg/dL) and creatinine (mg/dL) on experimental and test groups

Group	Urea $\bar{x} \pm Sx$	D.S.	Confidence level 95%	Creatinine $\bar{x} \pm Sx$	D.S.	Confidence level 95%
C_1	39.88 ± 0.05	1.55	1.25	0.62 ± 0.03	0.09	0.07
C_2	40.14 ± 0.59	1.57	1.25	0.63 ± 0.04	0.10	0.07
E_1	26.29 ±0.52*	1.38	1.25	0.6 ± 0.03^{ns}	0.08	0.07
E_2	29.57 ±0.75*	1.99	1.25	0.47 ±0.03*	0.08	0.07
E_3	26.86±0.40*	1.07	1.25	0.51±0.03**	0.09	0.07

E_1/C_2^{ns} – insignifican,*p<0.01, **p<0.05

The proteic metabolism exploration is useful especially in inflammatory, genetic and nutrition diseases and others [4]. Experimental studies with aspirin and others silicates revealed that this substance has many pharmacological actions, but it neither is nor clear if their actions are bounded to cell proteins [9]. Xenobiotics metabolisation can cause injury of hepatocytes with perturbation of cell function and form of reactive species of oxygen. Some by-products of salicylic acid can have baneful effects on liver [4]. Oxidative stress is one of the main mechanisms of chemical hepatotoxicity [1]. On rodents, in inflammatory processes were demonstrated the high produce of nitric oxide (NO) by INOX (induced synthetasys nitroxyd) from hepatocytes. Billiard and co. (1995) quoted by Dejica [1] has "in vitro" demonstrated on hepatocyte cultures that NO inhibit the proteic synthesis. This result is in contradiction with Frederich and co (1993) quoted by Dejica [1] that revealed "in vivo" capacity of NO to over-adjust the proteic synthesis in endotoxemy.

The albumin registered strong significant decreases (*p<0.01) in all experimental groups compared to test (E_1/C_2:-33.3%; E_2/C_2:-27.31%; E_3/C_2 :-32.08%) and under the physiological limits [8]. In the inflammatory system are registered decreases of albumin fractions. Serum albumin concentration decrease is produced in affections that lead to hepatic parenchyma damage because her synthesis is realized at hepatic level [4]. Hepatic parenchyma damage was accentuated also through AST and ALP transaminases determination in equal experimental conditions, consecutively to 5ClSA-SA, SA and SU administration [7]. In all the experimental groups, urea registered a strong significant decrease (p<0.01) compared to test (E_1/C_2: -34.5%; E_2/C_2: -33.8%; E_3/C_2: -33.08%) and under the physiological limits [5]. Urea determination is a way to appreciate the level of renal parenchyma affectation [4]. On 5ClSA-SA administration, the average values of creatinine was not significant (p>0.05) changed compared to test [8], but SA and SU administration has determinate strong significant decrease

($p<0.01$) respectively significant ($p<0.05$) compared to test, but the creatinine values was situated in physiological limits [8].

Conclusions

- The administration of 5ClSA-SA synthesis product determinate the increase of proteinemia over the physiological limits, while its basic structural compounds, SA and SU, induced proteinemia variations in physiological limits.
- Albumin and urea had registered significant decrease compared to test and to physiological limits consecutively to administration of the three used substances.
- Creatinine values has strong significant decrease compared to test but in physiological limits on SA and SU administration, and insignificant on 5ClSA-SA administration.

Bibliography

1. **Dejica,D.** (2000)-Oxidative stress in internal diseases, Ed.Casa Cărții de Ştiință, Cluj-Napoca
2. **Lupea, A.X., M., Pădure,** (2003) - Synthesis and characterization of some N-substituted Amides in Salicylic Acid Series, Rewiew of Research, Faculty of Sciences, Univ. of Novi Sad, 104, 5-10.
3. **Lupea,A.X., M.,Pădure, C.Tărăbășanu,** (2003) Synthesis and characterization of some N-substituted amides in 5-Chlorosalycilic Acid Series, Revista Chimie (Bucureşti) 54 (9), 752-756.
4. **Marin F**.(1995)-Clinic and morph functional explorations in medicine Ed. Tipomur, Târgu Mureş.
5. **Meingassner G., F.P., Schmook**. (1992) – Reference values for Crl:CD (SD)BR Rats –Sandoz-Research Institute, Viena,.
6. **Pădure,M.**(2003)-Studii pentru obținerea de noi derivați ai acidului salicilic cu aplicații în industria organică de sinteză fină, Timişoara, teza doctorat.
7. **Stana,L., A.,Trif, M.,Pădure, C.,Grăvilă, F.,Muselin, R., Ivancov** (2007)- Comparative study on the influence of some salicylic acid derivatives and sulfanilamide administration on serum transaminasis, Lucr. St. Zootehnie şi Biotehnologii, 40(1),183-188.
8. **Wilard D.M., H., Tveden, H.G.,Turnal (**1989) - Small clinical diagnosis By Laboratory methods , W.B.Saunders Company, Viena.
9. **Wu-Guo Deng, Ke-He Ruan, Min Du, M.A.,Saunders, K.Wu.,Kenneth (**2001)- Aspirin and salicylate immunoglobulin heavy chain binding protein and inhibit its ATPase activity in human fibroblast, The FASEB Journal,15,2463-2470.