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Synthesis of amino acid acetylsalicylates

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Abstract

Acetylsalicylic acid and its derivatives have different types of biological activity, including anti-aggregation, and are used as medications (for example, aspirin, *DL*-Lysine acetylsalicylate). Acetylsalicylic acid is slightly soluble in water and can be used only as an oral preparation, with This method of application leads to irritation of the gastric mucosa. When studying platelet aggregation, the condition of the platelet unit of the blood coagulation system is checked. Therefore, the synthesis and study of new antiplatelet agents with minimal side effects is an urgent task in solving the problem of preventing conditions associated with an increase in the thrombogenic potential of the blood.

To improve the method of introducing acetylsalicylic acid, we synthesized derivatives suitable for injections in the form of readily soluble in water (40% or more solubility) salts. This article presents the results of the study of the interaction of acetylsalicylic acid in aqueous acetone in a ratio of 1:4 with solutions of the corresponding amino acid in a molar ratio of 1:1. The reaction was monitored by TLC (ethanol-water mobile phase 1:1). The solution was then sterilized by bacterial filtration and evaporated to dryness. It has been shown that *L*-alaninium acetylsalicylate, *L*-proline acetylsalicylate, *D*-leucinium acetylsalicylate, *L*-ornithium acetylsalicylate, *L*-tyrosinium acetyl salicylate are formed. The individuality of the compounds obtained is confirmed by TLC data, and the structure is confirmed by IR and NMR data. In the structure of the synthesized compounds contains fragments of acetylsalicylic acid and amino acids, which allows them to have the presence of new fermaculic substances associated with the action of the amino acid component and the acetylisocyanate anion.

References

[1] A.A. Zheltova. Pharmacological correction of endothelial dysfunction and myocardial ischemia under conditions of experimental magnesium deficiency: Abstract. Dis. On competition of a scientific degree of the candidate of medical sciences. *Volgograd.* **2012**. P.24. (russian)
[2] K. Korttila, O.M. Pentti, J. Auvinen. Comparison of i.m. lysine acetylsalicylate and oxycodone in the treatment of pain after operation. *Br J Anaesth.* **1980**. Vol.52. No.6. P.613-27.
[3] C. Diaz, F.C. Gassó, J.N. Panadés. Double-blind study of the analgesic activity of fosfosal in patients with musculoskeletal and articular pain: comparison with lysine acetylsalicylate and placebo. *Clin Ther.* **1981**. Vol.4. No.2. P.121.
[4] J.F. Bretagne, A. Feuillu, M. Gosselin, J. Gastard. Aspirin and gastroduodenal toxicity. A double-blind endoscopic study of the effects of placebo, aspirin and lysine acetylsalicylate in healthy subjects]. *Gastroenterol Clin Biol.* **1984**. Vol.8. No.1. P.28-32.
[5] E.P. Gurfinkel, R. Altman, A. Scazziota, R. Heguilen, B. Mautner. Fast platelet suppression by lysine acetylsalicylate in chronicstable coronary patients. *Clin Cardiol.* **2000**. Vol.23. No.9. P.697-700.
[6] *U.S. PATENT* DOCUMENTS 2,101,867 12/1937 Miller et al 424/233 3,392,195 7/1968 Galat 424/233 Primary Examiner – Stanley J. Friedman Attorney, Agent, or Firm – Cushman, Darby & Cushman
[7] *PATENT US* 4265888 A61K31/615, 424/233 Acetylsalicylate powder preparation for injection. Y. Kagitani, T. Imagawa, H. Inahara, R. Watanabe; Assignee; The Green Cross Corporation. N110753; field; Jan. 8, *1980*; published May 5, **1981**.

[8] V.A. Ermokhin, M.V. Makarova. Synthesis of substituted *N*-(1-adamantil-1-carboxamido)- and *N*-(1-adamantilacetamido)-benzothiazoles. *Butlerov Communications.* **2013**. Vol.36. No.12. P.92-96. ROI: jbc-02/13-36-12-92
[9] A.S. Gilmutdinova, V.A. Ermokhin, P.P. Purygin, N.A. Klenova. Study of the derivatives of 1-adamantane carboxylic acid to induced platelet aggregation human in vitro. *Vestnik SSU*. **2015**. No.10 (132). P.143-150. (russian)
[10] A.K. Brel, S.V. Lisina. A.A. Spasov, and L.S. Mazanova. Esters of salicylic acid as a potential antipyretic. *Butlerov Communications.* **2009**. Vol.15. No.1. P.50-55. ROI: jbc-02/9-15-1-50