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Synthesis of new acyl derivatives of dihydroquercetin and catechin

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Abstract

Previously, it was shown that peracyl derivatives of dihydroquercetin (DHQ, taxifolin), including residues of aliphatic, aromatic and heterocyclic acids, had biological activity. In this work, peratsillirovanny dihydroquercetin containing nicotine fragment was synthesized.

Along with this, in order to expand the potential medicamentous effect, esters of DHA were obtained, simultaneously containing several different acyl pharmacophore residues. To this end, a tetraacylated DHA synthesized by a modified procedure containing a free hydroxyl group in the fifth position of the flavonoid fragment was synthesized. Subsequent acylation with acetylsalicylic acid and nicotinic acid chloride produced esters of various structures.

Also, in order to preserve the antioxidant activity, monoacyl substituted derivatives were synthesized. To accomplish this task, the previously synthesized acylated benzyl derivatives of catechin and the 3-isoxazolylbenzyl derivative obtained in this work were subjected to hydrogenation on a palladium catalyst. In this case, removal of benzyl protections was observed. It should be noted that acylation of tetrabenzyl catechin with isoxazolecarboxylic acid chloride was carried out under rather mild conditions. It should be emphasized that previously, the acylation with a reagent of tetrabenzylated dihydroquercetin under these conditions was not possible. Thus, presumably, the activity of the catechol fragment is related to the lack of an intramolecular hydrogen bond. After removal by hydrogenation of benzyl protecting protections, mono-derivatives of catechol containing an acyl residue of heterocyclic carboxylic acid in the third position of the flavonoid structure were synthesized.

As a result, the spectrum of biological activity was expanded while maintaining antioxidant properties. The structure of the obtained compounds was proved by NMR spectroscopy on ^{13}C, ^{1}H nuclei and elemental analysis.

References

[1] Yu.A. Tarakhovsky, Yu.A. Kim, B.S. Abdrasilov, E.N. Muzafarov Flavonoids: biochemistry, biophysics, medicine. *Pushchino: Synchrobook*. **2013**. 308p. (russian)
[2] G. Mikutis, H. Karakose, R. Jaiswal, et al. Phenolicpromiscuity in the cell nucleus – epigallocatechingallate (EGCG) and theaflavin-3,3-digallate from green and black tea bind to model cell nuclearstructures including histone proteins, double stranded DNA and telomeric quadruplex DNA. *Food Funct.* **2013**. Vol.2. P.328-337.
[3] J. Yang, l. Li, H. Jin et al. Vaginal gel formulation based on theflavin derivatives as a microbicide to prevent HIV sexual transmission. *AIDS Res. Hum. Retroviruses*. **2012**. Vol.28. P.1498-1508.
[4] R. Casado-Arroyo, C. Gargallo, A. Lanas. Balancing the risk and benefits of low-dose aspirin in clinical practice. *Best. Prac. Res. Clin. Gastroenterol.* **2012**. Vol.26. P.173-184.
[5] Derrys, Moore R.A. Single dose oral aspirin for acute postoperative pain in adults. *Cochrane. Datebase. Syst. Rev.* **2012**. 4. CD002067/

[6] B. Rocca, F. Santilli, D. Pitocco et al. The recovery of platelet cyclooxygenase activity explains interindividual variability in responsiveness to low-dose aCspirin in patients with and without diabetes. *J. Thromb. Haemost.* **2012**. Vol.10. P.1220-1230.
[7] I. Uriarte-Pueyo, M.I. Calvo. Flavonoids as acetilcholinesterase ingibitors. *Curr. Med. Chem.* **2011**. Vol.18. P.5289-5302.
[8] E.E. Nifant'ev, M.S. Krymchak, M.P. Koroteev, A.M. Koroteev, T.S. Kukhareva, L.K. Vasyanina. *Russ. J. Gen. Chem.* **2011**. Vol.81. No.1. P.102. DOI: 10.1134/S1070363211010154.
[9] V.S. Rogovsky, A.I. Matyushin, N.L. Shimanovsky, A.V. Semeikin, T.S. Kukhareva, A.M. Koroteev, M.P. Koroteev, E.E. Nifantiev. *Exp. and Wedge. Farm.* **2010**. No.9. P.39.
[10] E.E. Nifantiev, M.P. Koroteev, T.S. Kukhareva, A.M. Koroteev, N.M. Pugashova, S.E. Mosyurov, N.M. Kutuzova, G.Z. Kaziev. *Science and school.* **2012**. No.6. P.179.
[11] K. Freudenberg; K. Weinges. *Eur. Joc.* **1958**. Vol.613. No.1. P.61. DOI: 10.1002/jlac.19586130107.
[12] M.P. Koroteev, A.O. Pozdeev, and A.M. Koroteev. Acylation 5,7,3',4'-tetrabenzil catechin to heterocycles acid chlorides. *Butlerov Communications.* **2016**. Vol.48. No.11. P.18-22. ROI: jbc-02/16-48-11-18
[13] N. Salah, N.J. Mille, G. Paganga, L. Tijburg, G.P. Bolwell, C. Rice-Evans. *Arch. Biochem. Biophys.* **1995**. Vol.322. P.339. DOI: 10.1006/abbi.1995.1473.
[14] D.I. Tsimogiannis, V. Oreopoulou. *Innovative Food Science and Emerging Technologies.* **2004**. Vol.5. No.4. P.523. DOI:10.1016/j.ifset.2004.05.006
[15] A. Gordon, R. Ford. The chemist's companion. *Moscow: Mir.* **1976**. P.437.