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Study of the echinochrome stability and the products of its oxidative transformation

Key words: Echinochrome A, oxidative transformation

To ensure the quality of active pharmaceutical substances and finished drug products, impurities must be monitored carefully during process development, optimization, and process changeover. The isolation, characterization, and control of impurities in pharmaceutical substances are being reviewed with greater attention based on national regulatory and international guidelines.

Histochrome® is used in cardiological practice for the treatment of acute myocardial infarction and coronary heart diseases. Histochrome® is an effective medicine in ophthalmology and found a wide application in the treatment of corneal diseases for epithelialization acceleration, as well as retinal diseases such as a retinoprotector, at proliferative processes, of degenerations and different origin hemophthalmus. The active substance of the drug Histochrome® isechinochrome - 6-ethyl-2,3,5,6,7-pentahydroxynaphthaquinone (**1**). Due to the presence of a large number of phenolic hydroxyls, echinochrome is easily exposed to oxidative decomposition. In pharmaceuticals, the most common form of oxidative decomposition is auto-oxidation through a free-radical chain process.

Results from forced degradation studies of echinochrome in aqueous solution (pH 7.2) at room temperature we report here. A significant amount of the oxidation product (45-50%) was observed already 20 h after the beginning of the reaction. Products of the oxidation process **1** were identified using HPLC-DAD-MS (Shimadzu 2020).

Oxidation of **1** proceeded with the initial formation of dehydroechinochrome, the structure of which is established by NMR as 6-ethyl-2,3-dihydro-2,2,3,3,5,6,8-heptahydroxy-1,4-naphthoquinone (**2**) [1]. The high-resolution mass spectrum (ESI) of compound **2** exhibited a deprotonated molecular ion $[M–H]^-$ at *m*/*z* 299.0399 (calculated for $C_{12}H_{11}O_9$ 299.0409). The subsequent transformation of the unstable compound **2** with the elimination of CO_2 and H_2O and the cleavage of the C–C bond in the quinoid fragment gave ketoacids **3** and **4**. Carboxylic acids tend to lose carbon dioxide from the carboxyl groups during the isolation process. Therefore, to establish the structure of these compounds by NMR, stable methyl esters were obtained.

The relative retention times, absorption and mass spectra of compounds **2**-**4** were obtained.

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They will be used to develop a method for identifying impurities and determining the stability of substance and preparations based on echinochrome.

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