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Journal of the Serbian Chemical Society

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J. Serb. Chem. Soc. 73 (1) 127–129 (2008)
JSCS–3694

UDC 547.93:54+542.913.000.57+543+615
Book review

BOOK REVIEW

BILE ACIDS
Chemistry, biosynthesis, analysis, chemical and metabolic transformations and pharmacology

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Published by Mediset Publisher, Geneva, Switzerland, 2007, ISBN 0-12-045783-2

(Received 22 October 2007)

This book is published on 226 pages with 61 figures, 118 schemes, 10 tables and 689 references. It is divided into the following six chapters: 1. Introduction; 2. Structure and Origin of Bile Acids – An Overview; 3. Biosynthesis of Bile Acids in Mammalian Liver; 4. Isolation and Determination of Bile Acids; 5. Chemical and Metabolic Transformation of Selected Bile Acids; 6. Pharmacology of Bile Acids and Their Derivatives – Absorption Promoters and Therapeutic Agents. Figures, structures, reaction schemes and tables are clearly illustrated throughout the text.

In Chapter 1 (K. Kuhajda, J. Kandrač, S. Kevrešan, M. Mikov and J. P. Fawcett), an overview of the structure and origin of naturally occurring bile acids are given. The most dominant bile acids and their natural sources are summarized with a selection of naturally occurring bile acids with unusual structures, which have mostly been isolated from the bile of reptiles and amphibians.

The biosynthesis of bile acids in mammalian liver and its regulation together with physiological role of bile acids are reviewed in Chapter 2 (S. Kevrešan, K. Kuhajda, J. Kandrač, J. P. Fawcett and M. Mikov). A survey of the steps in the biosynthesis of bile acids from cholesterol in liver cells (hepatocytes) is given. Various mechanisms of the regulation of the biosynthesis of bile acids are presented. In addition to the physiological function of emulsifying lipids in the intestinal tract, the importance of the ability of bile acids to dissolve and transport cholesterol in the bile is emphasized.

In Chapter 3 (J. Kandrač, S. Kevrešan, M. Mikov, J. P. Fawcett and K. Kuhajda) the methods of isolation and determination of bile acids are reviewed. Methods for the separation of bile acids from cattle and pig bile are given in detail.

Isolation of a mixture of cholic and deoxycholic acids, as well as the purification of these acids from cattle bile is described. The isolation and purification of hyodeoxycholic acid and other components of pig bile are also described. Methods for the determination of bile acids in various biological samples are reviewed in several sections concerning enzyme assays, radioimmunoassay, enzyme immunoassay and chromatographic methods. Among the chromatographic methods, the separation and determination of bile acids by thin-layer chromatography, gas chromatography, gas-liquid chromatography and high performance liquid chromatography are reviewed. Particular attention is given to high performance liquid chromatography methods, which have recently been the most often applied methods of the separation and determination of bile acids.

Chapter 4 (K. Kuhajda, S. Kevrešan, J. Kandrač, J. P. Fawcett and M. Mikov) gives a survey of chemical transformations of selected bile acids. The first chemical transformations of bile acids were performed with the aim of determining their structure, and later they were concerned with transformations of particular bile acids to other bile acids, as well as with the syntheses of steroid hormones and some vitamins. To this end, use was mostly made of the reactions of selective acylation, oxidation and reduction of selected bile acids and their derivatives. The papers dealing with the synthesis of potential metabolites in the biosynthesis of bile acids are also herein presented. Steroid hormones, such as pregnenolone, progesterone and testosterone, are synthesized from methyl hyodeoxycholate, and cortisone from methyl deoxycholate. Numerous works and patents devoted to the synthesis of ursodeoxycholic acid from cholic or chenodeoxycholic acid indicate its effectiveness in the treatment of cholelithiasis. Chenodeoxycholic acid appears to be an excellent precursor in the synthesis of a steroid plant growth regulator, as well as in the syntheses of metabolites and vitamin D analogues. Chirality of bile acids can be used in the syntheses of cyclic and acyclic molecular chiral receptors and chiral solvents. Cholic and deoxycholic acids serve in the creation of new macrocyclic structures, which exhibited different capacities in binding and transporting other compounds. Also, one of the trends in the chemistry of bile acids is their application in combinatorial chemistry.

M. Mikov, J. P. Fawcett, K. Kuhajda and S. Kevrešan review the pharmacology of bile acids and their derivatives in Chapter 5. The therapeutic use of bile has been recognized since ancient times. Previously bile acids were the standard treatment for gallstones, chenodeoxycholic acid and ursodeoxycholic acid are effective in causing the dissolution of cholesterol gallstones in humans, but today their therapeutic role looks set to expand enormously. Bile acids as absorption promoters have the potential to aid intestinal, buccal, transdermal, ocular, nasal, rectal and pulmonary absorption of various drugs. Keto derivatives of cholic acid, 3α,7α-dihydroxy-12-keto-5α-cholic acid (sodium salt and methyl ester) are potential modifiers of the blood-brain barrier, and it was found that they pro-

moted quinine uptake, enhanced the analgesic effect of morphine and prolonged the sleeping time induced by pentobarbital. The barriers to the administration of drugs by these routes can be overcome by bile acids at concentrations that are non-toxic. Bile acids as therapeutic agents have the potential to produce beneficial effects in sexually transmitted diseases, primary biliary cirrhosis, primary sclerosing cholangitis, gallstones, digestive tract diseases, cystic fibrosis and cancer.

In conclusion, this is an extremely useful text for anyone involved in bile acids, teaching or research. In my opinion, no better comprehensive treatise of this subject exists. The book may also serve as a good reference source for those contributing to further developments in this field. For those who are looking for a new area of research that can have an impact on the public health, this text offers an excellent place to begin. The editors and their collaborators are to be commended on their efforts in bringing this field to our attention.

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