

## 综述

### 醛糖还原酶的研究进展

谷娟<sup>1</sup>, 严谨<sup>2</sup>, 吴卫华<sup>3, 4</sup>, 黄琪<sup>3</sup>, 欧阳冬生<sup>1</sup>

1.中南大学临床药理研究所, 长沙 410078; 2.中南大学湘雅三医院护理部, 长沙 410013;  
3.中南大学药学院, 长沙 410078; 4.怀化医学高等专科学校药理学系, 湖南 怀化 418000

摘要:

醛糖还原酶是醛-酮还原酶超家族的一员, 广泛存在于血管、肾脏、心脏、脑、骨骼肌、视网膜、胎盘、神经等组织中。它以烟酰胺腺嘌呤二核苷酸(NADPH)为辅酶催化多种醛、酮类物质还原为醇。除促进糖尿病并发症发生外, 还参与多种氧化应激性疾病, 参与细胞信号转导和细胞增殖过程。

关键词: 醛糖还原酶 功能 活性 疾病 抑制剂

### Research progress in aldose reductase

GU Juan<sup>1</sup>, YAN Jin<sup>2</sup>, WU Weihua<sup>3,4</sup>, HUANG Qi<sup>3</sup>, OUYANG Dongsheng<sup>1</sup>

1.Institute of Clinical Pharmacology, Central South University, Changsha 410078; 2.Nursing Department, Third Xiangya Hospital, Central South University, Changsha 410013;  
3.Pharmacy College, Central South University, Changsha 410078; 4.Department of Pharmacy, Huaihua Medical College, Huaihua Hunan 418000, China

Abstract:

Aldose reductase is a member of aldehyde-keto reductase superfamily widely existing in the kidney, adrenal gland, lens, retina, nerve, heart, placenta, brain, skeletal muscle, testis, blood vessels, lung, liver, et al. It is a reduced nicotinamide-adenine dinucleotide phosphate (NADPH)-dependent enzyme catalyzing the reduction of various aldehydes and ketones to the corresponding alcohol. It is involved in many oxidative stress diseases, cell signal transduction and cell proliferation process as well as diabetes complications. In recent years, some progress has been made in research of the activity and gene regulation of aldose reductase and the relation with many common diseases.

Keywords: aldose reductase; function; activity; diseases; inhibitor

收稿日期 2009-06-22 修回日期 网络版发布日期

DOI: 10.3969/j.issn.1672-7347.2010.

基金项目:

通讯作者: 欧阳冬生

作者简介:

作者Email: ouyangyj@163.com

### 参考文献:

- [1] O'connor T, Ireland L S, Harrison D J, et al. Major differences exist in the function and tissue-specific expression of human aflatoxin B1 aldehyde reductase and the principal human aldo-keto reductase AKR1 family members [J]. Biochem J, 1999, 343(2):487-504.
- [2] Lee K W Y, Ko B C B, Jiang Z, et al. Overexpression of aldose reductase in liver cancers may contribute to drug resistance [J]. Anti-Cancer Drugs, 2001, 12(2): 129-132.
- [3] Lefrançois-Martinez A M, Bertherat J, Val P, et al. Decreased expression of cyclic adenosine monophosphate-regulated aldose reductase (AKR1B1) is associated with malignancy in human sporadic adrenocortical tumors [J]. J Clin Endocrinol Metab, 2004, 89 (6): 3010-3019.
- [4] Anil Kumar P, Bhanuprakash Reddy G. Focus on Molecules: Aldose reductase [J]. Exper Eye Res, 2007, 85(6):739-740.
- [5] Wilson D K, Bohren K M, Gabbay K H, et al. An unlikely sugar substrate site in the 1.65 Å structure of the human aldose reductase holoenzyme Implicated in diabetic complications [J]. Science, 1992, 257 (5066):81-84.

扩展功能

本文信息

▶ Supporting info

▶ PDF(1081KB)

▶ [HTML全文]

▶ 参考文献[PDF]

▶ 参考文献

服务与反馈

▶ 把本文推荐给朋友

▶ 加入我的书架

▶ 加入引用管理器

▶ 引用本文

▶ Email Alert

▶ 文章反馈

▶ 浏览反馈信息

本文关键词相关文章

▶

▶ 醛糖还原酶

▶ 功能

▶ 活性

▶ 疾病

▶ 抑制剂

本文作者相关文章

PubMed

- [6] Rondaw J M, Tete-Favier F, Podjarny A, et al. Novel NADPH-binding domain revealed by the crystal structure of aldose reductase [J] . *Nature*, 1992, 30(335):469-472.
- [7] Hers H G. The mechanism of the transformation of glucose in fructose in the seminal vesicles [J] . *Biochim Biophys Acta*, 1956, 22 (1):202-203.
- [8] Burg M B, Kwon E D, Kultz D. Regulation of gene expression by hypertonicity [J] . *Ann Rev Physiol*, 1997, 59: 437-455.
- [9] Srivastava S, Chandra A, Bhatnagar A, et al. Ansari NH. Lipid peroxidation product, 4-hydroxynonenal and its conjugate with GSH are excellent substrates of bovine lens aldose reductase [J] . *Biochem Biophys Res Commun*, 1995,217(3):741-746.
- [10] Vander Jagt D L, Kolb N S, Vander Jagt T J, et al. Substrate specificity of human aldose reductase: identification of 4-hydroxynonenal as an endogenous substrate [J] . *Biochim Biophys Acta*, 1995, 1249 (2):117-126.
- [11] Srivastava S, Watowich S J, Petrash J M, et al. Structural and kinetic determinants of aldehyde reduction by aldose reductase [J] . *Biochemistry*, 1999, 38(1):42-54.
- [12] Ramana K V, Dixit B L, Srivastava S, et al. Selective recognition of glutathiolated aldehydes by aldose reductase [J] . *Biochemistry*, 2000,39(40):12172-12180.
- [13] Bhatnagar A, Srivastava S K. Aldose reductase: congenial and injurious profiles of an enigmatic enzyme [J] . *Biochem Med Metab Biol*, 1992, 48(2):91-121.
- [14] Petrash J M, Harter T M, Murdock G L. A potential role for aldose reductase in steroid metabolism [J] . *Adv Exp Med Biol*, 1997,414:465-473.
- [15] Wermuth B, Monder C. Aldose and aldehyde reductase exhibit isocorticosteroid reductase activity [J] . *Eur J Biochem*, 1983,131(2):423-426.
- [16] Srivastava S K, Hair G A, Das B, et al. activated and unactivated forms of human erythrocyte aldose reductase [J] . *Proc Natl Acad Sci USA*, 1985, 82(21):7222-7226.
- [17] Chandra A, Srivastava S, Petrash J M, et al. Active site modification of aldose reductase by nitric oxide donors [J] . *Biochimica et Biophysica Acta*, 1997,1341(2):217-222.
- [18] Hwang Y C, Sato S, Tsai J Y, et al. Aldose reductase activation is a key component of myocardial response to ischemia [J] . *FASEB J*, 2002,16 (2):243-245.
- [19] Baba S P, Wetzelberger K, Hoetker J D, et al. Posttranslational glutathiolation of aldose reductase (AKR1B1): A possible mechanism of protein recovery from S-nitrosylation [J] . *Chem Biol Interact*, 2009, 178 (1-3):250-258.
- [20] Chang K C, Paek K S, Kim H J, et al. Substrate-induced up-regulation of aldose reductase by methylglyoxal, a reactive oxoaldehyde elevated in diabetes [J] . *Mol Pharmacol*, 2002,61(5):1184-1191.
- [21] Hontta N, Akanuma Y, Kawamori R, et al. Long-term clinical effects of epalrestat, an aldose reductase inhibitor, on diabetic peripheral neuropathy. The 3-year, multicenter, comparative aldose reductase inhibitor-diabetes complications trial [J] . *Diabetes Care*, 2006, 29(7):1538-1544.
- [22] Ramirez M A, Borja N L. Epalrestat: an aldose reductase inhibitor for the treatment of diabetic neuropathy [J] . *Pharmacotherapy*, 2008, 28(5):646-655.
- [23] Hotta N, Toyota T, Matsuoka K, et al. Clinical efficacy of fidarestat, a novel aldose reductase inhibitor, for diabetic peripheral neuropathy: a 52-week multicenter placebo-controlled double-blind parallel group study [J] . *Diabetes Care*, 2001, 24(10):1776-1782.
- [24] Jung H A, Yoon N Y, Bae H J, et al. Inhibitory activities of the alkaloids from *Coptidis Rhizoma* against aldose reductase [J] . *Arch Pharm Res*, 2008,31 (11):1405-1412.
- [25] Fatmawati S, Kurashiki K, Takeno S, et al. The inhibitory effect on aldose reductase by an extract of *Ganoderma lucidum* [J] . *Phytother Res*, 2008, 23 (1):28-32.
- [26] 吕立华, 吕林华, 欧阳冬生. 20种天然降压化合物对醛糖还原酶抑制作用的研究 [J] . *中医药导报*, 2008, 14 (10):8-12.
- L Lihua, L Linhua, OUYANG Dongsheng. The study of twenty natural antihypertensive compound' s aldose reductase inhibition [J] . *Guiding Journal of Tradittonal Chinese Medicing and Pharmacy*, 2008, 14(10):8-12.
- [27] Wang Y, Lee S C, So W Y, et al. Phenotypic heterogeneity and associations of two aldose reductase gene polymorphisms with nephropathy and retinopathy in type 2 diabetes [J] . *Diabetes Care*, 2003, 26 (8):2410-2415.
- [28] Kador P F. Contributions of Jin H. Kinoshita to aldose reductase research [J] . *Exp Eye Res*, 1990, 50 (6):615-620.
- [29] Williamson J R, Chang K, Frangos M, et al. Hyperglycemic pseudohypoxia and diabetic complications [J] . *Diabetes*, 1993, 42 (6):801-813.
- [30] 吴静, 钟慧菊, 孙志湘, 等. 灯盏花素治疗糖尿病周围神经病变的疗效观察 [J] . *湖南医科大学学报*, 2002, 27(4):337-339.
- WU Jing, ZHONG Huiju, SUN Zhixiang, et al. Observation of therapeutic effect of breviscapine on diabetic peripheral neuropathy [J] . *Bulletin of Hunan Medical University*, 2002, 27(4):337-339.
- [31] 刘长山, 朱禧星. 糖尿病患者红细胞醛糖还原酶活性的初步观察 [J] . *糖尿病杂志*, 1996, 4 (4):198-201.
- LIU Changshan, ZHU Xixing. Initial observation of erythrocyte aldose reductase activity in Diabetes [J] . *Chinese Journal of Diabetes*, 1996, 4 (4):198-201.
- [32] Ramana K V, Chandra D, Srivastava S, et al. Aldose reductase mediates mitogenic signaling in

vascular smooth muscle cells [J]. J Biol Chem, 2002, 277(35): 32063-32070.

[33] 欧阳冬生, 黄琪, 刘黎, 等. 醛糖还原酶在糖尿病并发症和心血管病变中的作用 [J]. 中国现代医学杂志, 2008, 18 (17): 2506-2509.

OUYANG Dongsheng, HUANG Qi, LIU Li, et al. Role of aldose reductase in diabetic complications and angiocardopathy [J]. China Journal of Modern Medicine, 2008, 18 (17): 2506-2509.

[34] 车祺, 蒋涛, 林伊凤, 等. 醛糖还原酶基因转染对体外培养大鼠肾脏系膜细胞增殖的影响 [J]. 中?土咯r又? 2005, 34(7): 417-420.

CHE Qi, JIANG Tao, LIN Yifeng, et al. Effects of aldose reductase transfection on the proliferation of rat mesangial cells in vitro [J]. Chinese Journal of Pathology, 2005, 34(7): 417-420.

[35] Papezizikova I, Pekarova M, Chatzopoulou M, et al. The effect of aldose reductase inhibition by JMC-2004 on hyperglycemia-induced endothelial dysfunction [J]. Neuro Endocrinol Lett, 2008, 29 (5): 775-778.

[36] Vikramadithyan R K, Hu Y, Noh H L, et al. Human aldose reductase expression accelerates diabetic atherosclerosis in transgenic mice [J]. J Clin Invest, 2005, 115(9): 2434-2443.

[37] Ramasamy R, Oates P J, Schaefer S. Aldose reductase inhibition protects diabetic and nondiabetic rat hearts from ischemic injury [J]. Diabetes, 1997, 46(2): 292-300.

[38] 郑春华, 周利, 陈园, 等. 醛糖还原酶拮抗剂治疗大鼠血管再狭窄 [J]. 中华高血压杂志, 2007, 15(8): 651-655.

ZHENG Chunhua, ZHOU Li, CHEN Yuan, et al. Aldose reductase inhibitor and blood vessel restenosis [J]. Chinese Journal of Hypertension, 2007, 15(8): 651-655.

[39] Srivastava S, Chandrasekar B, Bhatnagar A, et al. Lipid peroxidation-derived aldehydes and oxidative stress in the failing heart: role of aldose reductase [J]. Am J Physiol, 2002, 283: H2612-H2619.

[40] Ruef J, Liu S Q, Bode C, et al. Involvement of aldose reductase in vascular smooth muscle cell growth and lesion formation after arterial injury [J]. Arterioscler Thromb Vasc Biol, 2000, 20: 1745-1752.

[41] Liu X, Shen J, Zhan R, et al. Proteomic analysis of homocysteine induced proliferation of cultured neonatal rat vascular smooth muscle cells [J]. Biochim Biophys Acta, 2009, 1794 (2): 177-184.

[42] Ananthakrishnan R, Kaneko M, Hwang Y C, et al. Aldose reductase mediates myocardial ischemia-reperfusion injury in part by opening mitochondrial permeability transition pore [J]. Am J Physiol Heart Circ Physiol, 2009, 296 (2): H333-H341.

[43] Keith R J, Haberkzetti P, Vladykovskaya E, et al. Aldose reductase decreases endoplasmic reticulum stress in ischemic hearts [J]. Chemico-Biological Interactions, 2009, 178 (1-3): 242-249.

[44] Srivastava S K, Ramana K V, Bhatnagar A. Role of aldose reductase and oxidative damage in diabetes and the consequent potential for therapeutic options [J]. Endocr Rev, 2005, 26 (3): 380-392.

[45] Kabututu Z, Manin M, Pointud J C, et al. Prostaglandin F<sub>2</sub>{alpha} synthase activities of aldo-keto reductase 1B1, 1B3, 1B7 [J]. J Biochem, 2009, 145 (2): 161-168.

[46] Tammali R, Ramana K V, Singhal S S, et al. Aldose reductase regulated growth factor-induced cyclooxygenase-2 expression and prostaglandin E<sub>2</sub> production in human colon cancer cells [J]. Cancer Res, 2006, 66 (19): 9705-9713.

#### 本刊中的类似文章

1. 李婷<sup>1,2</sup>, 周建华<sup>1</sup>, 邓征浩<sup>1</sup>, 傅春燕<sup>1</sup>, 蒋海鹰<sup>1</sup>, 高振芹<sup>1</sup>, 王金胜<sup>2</sup>, 任宏政<sup>1</sup>, 王鹏<sup>1</sup>. FGF-2和osteopontin在非小细胞肺癌中的表达及其相关性[J]. 中南大学学报(医学版), 2009, 34(11): 1114-1119
2. 谭倩<sup>1</sup>, 唐华容<sup>1</sup>, 刘荣荣<sup>2</sup>, 王光平<sup>1</sup>, 杨晓苏<sup>3</sup>, 陈方平<sup>1</sup>. FVII活化蛋白酶基因的Marburg I型多态性与脑梗死发病的相关性[J]. 中南大学学报(医学版), 2009, 34(12): 1171-1175
3. 谭洪毅, 潘频华, 赵然然, 覃庆武, 王慧, 胡成平. 呼吸道合胞病毒感染大鼠脊髓背根节信号转录因子的研究[J]. 中南大学学报(医学版), 2009, 34(12): 1189-1195
4. 袁平, 王万春. 膝关节三维有限元模型的建立及生物力学分析[J]. 中南大学学报(医学版), 2010, 35(1): 85-89
5. 王微微<sup>1, 2</sup>, 张明<sup>1</sup>, 王渊<sup>1</sup>, 金晨望<sup>1</sup>, 闫斌<sup>1</sup>, 麻少辉<sup>1</sup>. 脑内5-HT参与S I及S II脑区痛觉调控的功能磁共振成像研究[J]. 中南大学学报(医学版), 2010, 35(3): 185-193
6. 卿春华, 陈平, 向旭东. 茶多酚对低剂量烟草悬凝物诱导人支气管上皮细胞氧化损伤及凋亡的影响[J]. 中南大学学报(医学版), 2010, 35(2): 123-
7. 吕梁<sup>1</sup>, 霍继荣<sup>1</sup>, 刘佳<sup>2</sup>, 武捷<sup>2</sup>, 王捷<sup>2</sup>. APC不同功能区域对结肠癌细胞株HT-29中β-连环蛋白表达的影响[J]. 中南大学学报(医学版), 2010, 35(2): 140-
8. 杨乐平, 谭兴国, 杨竹林, 李清龙, 苗雄鹰. 胰腺癌大鼠RAD51和MAX的表达[J]. 中南大学学报(医学版), 2010, 35(2): 146-
9. 王敏<sup>1</sup>, 李先平<sup>1</sup>, 王庆林<sup>2</sup>, 汤兰桂<sup>2</sup>. 用抗HCV多抗从随机12肽库中筛选抗原表位[J]. 中南大学学报(医学版), 2010, 35(3): 236-240
10. 樊敏<sup>1</sup>, 刘伏友<sup>2</sup>, 杨宇<sup>1</sup>, 叶云<sup>1</sup>, 黄谷香<sup>1</sup>. 糖原合成酶激酶-3β磷酸化促进人腹膜间皮细胞转分化的实验研究[J]. 中南大学学报(医学版), 2010, 35(4): 329-
11. 王文欢<sup>1</sup>, 伍仁毅<sup>1</sup>, 孙国璜<sup>2</sup>, 李新华<sup>1</sup>, 袁伟建<sup>1</sup>, 唐丽安<sup>1</sup>. VEGF-C和VEGF-D在胃癌组织中的表达与淋巴结转移的关系[J]. 中南大学学报(医学版), 2010, 35(4): 335-
12. 刘虹, 彭佑铭, 李娟, 刘映红, 成梅初, 袁芳, 刘伏友. 3547例慢性肾脏疾病患者分期及相关因素分析[J]. 中南大学学报(医学版), 2010, 35(5): 499-
13. 陶立坚<sup>1</sup>, \*, 张军<sup>1</sup>, 胡高云<sup>2</sup>, 陈卓<sup>2</sup>, 龚娟<sup>2</sup>. 1-(3-氟苯基)-5-甲基-2-(1H)吡啶酮对鼠肾成纤维细胞的影

响[J]. 中南大学学报(医学版), 2004,29(2): 139-141

14. 陈名久, 吴显宁, 尹邦良, 等.可吸收线分层缝合法在颈部食管胃吻合术中的应用[J]. 中南大学学报(医学版), 2011,36(3): 265-

15. 朱淑娟<sup>1, 2</sup>, 钱亦华<sup>1</sup>, 史利利<sup>1</sup>, 杨维娜<sup>1</sup>, 冯新正<sup>1</sup>, 李翠琴<sup>3</sup>, 刘勇<sup>1</sup>.丹参酮IIA对A $\beta$ 25-35引起的Meynert核团

神经元钙电流变化的影响[J]. 中南大学学报(医学版), 2010,35(8): 840-

---

Copyright by 中南大学学报(医学版)