Remedy Open Access

Editorial
Published: 25 Nov, 2016

Cyclodextrins: Going from Supporting Role to Leading Actor

*Ao M[1,2] and Chen Y[1,3]**

[1]*College of Life Sciences, Nanchang University, P.R. China*

[2]*Department of Pharmacy, Jiangxi University of Traditional Chinese Medicine, P.R. China*

[3]*Nanoscale Science and Technology Laboratory, Nanchang University, P.R. China*

Editorial

Cyclodextrins (CDs) are a family of cyclic oligosaccharides composed of 5 or more α-(1,4)-linked glucopyranose subunits among which α-, β-, and γ-cyclodextrin (consisting of six, seven, and eight glucopyranose subunits in a ring, respectively) are the three major types. After more than a hundred years of research since first discovered, cyclodextrins have been structurally and chemically characterized and widely applied in food, pharmaceutical and others playing supporting roles (e.g. as a delivery system of foods or drugs).

Interestingly, cyclodextrins are gradually going from supporting role to leading actor since in recent years it was found that cyclodextrins per se could be recruited as effective drugs for several diseases. The specific structural property of cyclodextrins (i.e. hydrophobic inside and hydrophilic outside) helps not only to host food/drug molecules as a delivery system but also to extract lipids (particularly cholesterol) from diseased tissues/cells as a potential drug.

Well characterized are the effects of hydroxypropyl-beta-cyclodextrin (HPβCD), a derivative of β-CD, on Niemann-Pick type C (NPC) disease and an autosomal recessive disorder characterized by intracellular cholesterol accumulation, gliosis and neuronal loss in selected brain regions. Accumulating evidence proved that HPβCD can prevent neurodegenerative changes in $NPC1^{-/-}$ mice [1-4]. HPβCD has received orphan drug designation for the treatment of NPC disease. It was also showed that HPβCD has neuroprotective effects on Alzheimer disease which shares neuropathological features with NPC [5]. Methy-beta-cyclodextrin (MβCD), another derivative of β-CD, also has been reported to have antitumor effects via cholesterol depletion from lipid rafts in the plasma membrane of tumor cells [6-8].

Most recently, the potentially anti-atherosclerotic effects of cyclodextrins were evaluated. Zimmer et al. [9] reported that HPβCD could mediate regression of atherosclerotic plaques *in vivo* potentially by solubilizing extracellular and intracellular cholesterol crystals and increasing cholesterol efflux from macrophages *in vitro*. Our *in vivo* experimental data also shows that HPβCD can inhibit the progression of atherosclerosis (unpublished data). On the other hand, we revealed that cyclodextrins including α-CD, γ-CD, HPβCD and MβCD could alter the structures of low-density lipoprotein (LDL) and high-density lipoproteins (HDL; unpublished data) and inhibit LDL/HDL oxidation [10]. We also found that MβCD could inhibit the adhesion of monocytes onto endothelial cells by down-regulating adhesion molecules and caveolae [11]. Therefore, it seems that cyclodextrins could inhibit or even reverse the progression of atherosclerosis potentially via mutiple mechanisms correlating with different key steps during atherogenesis including LDL/HDL oxidation, monocyte-endothelium adhesion, solubilization of cholesterol crystals, cholesterol efflux, among others.

Cyclodextrins are produced from starch via enzymatic conversion and have already been recognized as safe by the FDA. Therefore, the role switching of cyclodextrins from a drug delivery system to a commercial drug may be relatively easier and smoother than the development of a traditional new drug. For inclusion complexes of cyclodextrins with other drugs, cyclodextrins could be regarded as not only a drug carrier but a combination drug for combination therapy. For example, the cyclodextrin inclusion compounds of an antitumor drug may be used to treat cancer and atherosclerosis simultaneously. In the future, more attention should be placed on developing drug efficacy of cyclodextrins while applying their drug-delivery capability.

OPEN ACCESS

Correspondence:
Yong Chen, Nanoscale Science and Technology Laboratory, Institute for Advanced Study, Nanchang University, 999 Xuefu Ave., Honggutan District, Nanchang, Jiangxi 330031, China, Tel: 86-791-83969963; Fax: 86-791-83969963;
E-mail: dr_yongchen@hotmail.com

Received Date: *18 Sep 2016*
Accepted Date: *22 Nov 2016*
Published Date: *25 Nov 2016*

Citation:
Ao M, Chen Y. Cyclodextrins: Going from Supporting Role to Leading Actor. Remed Open Access. 2016; 1: 1030.

References

1. Ramirez CM, Liu B, Taylor AM, Repa JJ, Burns DK, Weinberg AG, et al. Weekly cyclodextrin administration normalizes cholesterol metabolism in nearly every organ of the Niemann-Pick type C1 mouse and markedly prolongs life. Pediatr Res. 2010; 68: 309-15.
2. Aqul A, Liu B, Ramirez CM, Pieper AA, Estill SJ, Burns DK, et al. Unesterified cholesterol accumulation in late endosomes/lysosomes causes neurodegeneration and is prevented by driving cholesterol export from this compartment. J Neurosci. 2011; 31: 9404-9413.
3. Maulik M, Ghoshal B, Kim J, Wang Y, Yang J, Westaway D, et al. Mutant human APP exacerbates pathology in a mouse model of NPC and its reversal by a beta-cyclodextrin. Hum Mol Genet. 2012; 21: 4857-4875.
4. Vance JE, Karten B. Niemann-Pick C disease and mobilization of lysosomal cholesterol by cyclodextrin. J Lipid Res. 2014; 55: 1609-1621.
5. Yao J, Ho D, Calingasan NY, Pipalia NH, Lin MT, Beal MF. Neuroprotection by cyclodextrin in cell and mouse models of Alzheimer disease. J Exp Med. 2012; 209: 2501-2513.
6. Grosse PY, Bressolle F, Vago P, Simony-Lafontaine J, Radal M, Pinguet F. Tumor cell membrane as a potential target for methyl-beta-cyclodextrin. Anticancer Res. 1998; 18: 379-384.
7. Grosse PY, Bressolle F, Pinguet F. Antiproliferative effect of methyl-beta-cyclodextrin *in vitro* and in human tumour xenografted athymic nude mice. Br J Cancer. 1998; 78: 1165-1169.
8. Gotoh K, Kariya R, Alam MM, Matsuda K, Hattori S, Maeda Y, et al. The antitumor effects of methyl-beta-cyclodextrin against primary effusion lymphoma via the depletion of cholesterol from lipid rafts. Biochem Biophys Res Commun. 2014; 455: 285-289.
9. Zimmer S, Grebe A, Bakke SS, Bode N, Halvorsen B, Ulas T, et al. Cyclodextrin promotes atherosclerosis regression via macrophage reprogramming. Sci Transl Med. 2016; 8: 333ra50.
10. Ao M, Gan C, Shao W, Zhou X, Chen Y. Effects of cyclodextrins on the structure of LDL and its susceptibility to copper-induced oxidation. Eur J Pharm Sci. 2016; 91: 183-189.
11. Ao M, Wu L, Zhou X, Chen Y. Methyl-beta-Cyclodextrin Impairs the Monocyte-Adhering Ability of Endothelial Cells by Down-Regulating Adhesion Molecules and Caveolae and Reorganizing the Actin Cytoskeleton. Biol Pharm Bull. 2016; 39: 1029-1034.