Choline Phospholipids to Transport Docosahexaenoic Acid to the Brain

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Docosahexaenoic acid (DHA) is a major polyunsaturated fatty acid (PUFA) in the brain and retina where it plays a crucial role in brain development, learning ability and visual acuity. Also, several neurodegenerative disorders have been associated with a decreased brain DHA content. It is assumed that most of this PUFA is crossing the blood brain barrier from blood plasma for the brain accretion, and it has been suggested that *sn*-2-docosahexaenoyl-glycero-phosphocholine (*sn*-2 LysoPC-DHA) is around 10-fold more efficient than the non-esterified form of DHA to provide DHA to this organ, in contrast to what has been observed in some other organs. However, *sn*-2 LysoPC-DHA readily isomerizes into the *sn*-1 isomer to reach approximately the 4/1 ratio for *sn*-1/*sn*-2 at the equilibrium. Assuming that *sn*-2 LysoPC-DHA is the physiological form to be re-esterified at the sn-1 position in the target tissue, we aimed at preventing the *sn*-2/*sn*-1 isomerization by adding the shortest possible acyl chain at the *sn*-1 position of LysoPC-DHA to keep most of the LysoPC properties. This can be done either by chemical acetylation of *sn*-2 LysoPC-DHA or by one-step transesterification of DHA-containing PC in presence of an acetyl donor. The resulting phospholipid, called AceDoPC, is assessed *in vivo* for its biological relevance.