GLUCOSE-BASED CHOLINESTERASES INHIBITORS

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Neurodegenerative diseases are closely associated with dysfunction of the cholinergic system, in which acetylcholine (ACh) acts as the primary neurotransmitter responsible for transmitting electrical impulses between nerve cells. In patients with Alzheimer's disease (AD), acetylcholine levels rapidly decrease due to excessive hydrolysis by acetylcholinesterase (AChE). Butyrylcholinesterase (BChE) is another enzyme closely related to AChE, it functions like a co-regulator of cholinergic system by hydrolysing ACh. Increased activity of BChE in the temporal cortex and the hippocampus is seen in patients with progressive AD. Focusing on both of these enzymes is important due to their different locations, AChE predominantly localised in the central nervous system, whereas BChE is present more in the peripheral tissues. [1] In this study, different glucose-6-esters were synthesised and their potential inhibitory effects on cholinesterases were evaluated. Glucose-6-esters were synthesised by a transesterification reaction catalysed by Candida antarctica lipase B (CALB). During a transesterification reaction one ester is converted into another ester through its reaction with an alcohol. In this case, a regioselective enzyme CALB was used to ensure selective modification of only the primary alcohol group of glucose. The acyl group was transferred from a short-chain vinyl ester, which were selected as acyl group donors. The reaction is driven towards product formation by spontaneous tautomerization of alcohol by-product into acetaldehyde, rendering the process irreversible consequently maximising product yield. [2] The main objective of this study was to use amperometric biosensors to measure the inhibitory effects of the synthesised glucose-6-esters on cholinesterase activity. Esterase activity was estimated using immobilised choline oxidase. In this system, ACh is hydrolysed by AChE to produce choline, which subsequently is oxidised by choline oxidase to generate hydrogen peroxide (H_2O_2). The peroxide undergoes oxidation at a platinum electrode, producing an amperometric signal directly proportional to the amount of peroxide formed. For the synthesis of glucose-6-esters, seven different short-chain vinyl esters were used: vinyl acetate, vinyl propionate, vinyl propionate, vinyl methacrylate, vinyl pivalate, vinyl 4-tert-butylbenzoate and vinyl benzoate. To determine synthesis efficiency two analytical methods were used, amperometric glucose biosensor and DNS method for reducing sugars. During the synthesis process, glucose is consumed, and its depletion, measured by the glucose biosensor, directly correlates with the quantity of ester product formed. The results showed that glucose-6-esters containing longer acyl chains provided more effective inhibition of cholinesterases. However, only three out of seven glucose-6-esters (acetate, propionate, butyrate) were obtained during the synthesis process with CALB.

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[2] J. F. Kennedy et al., "Enzyme-catalyzed regioselective synthesis of sugar esters and related compounds," Journal of Chemical Technology & Biotechnology, vol. 81, no. 6, pp. 866–876, Apr. 2006, doi: 10.1002/jctb.1473.