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Effects of alimemazine, cyamemazine, propericiazine trihexyphenidyl and lithium on the sphingomyelinase activity of cultured human fibroblasts

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Sphingomyelin is a phospholipid which plays an important structural and physiological role in cellular membranes and especially myelin. An increase in sphingomyelin content has been reported in erythrocyte membranes of schizophrenic patients. Sphingomyelinase, which catabolizes sphingomyelin, is decreased in glioma cells and human cultured fibroblasts, under the influence of tricyclic antidepressants and phenothiazines. In the present study, human cultured fibroblasts were incubated for 24 hours in the presence of phenothiazines (alimemazine, cyamemazine and propericiazine), an anticholinergic drug (trihexyphenidyl hydrochloride) and lithium carbonate. Lithium carbonate alimemazine tartrate and trihexyphenidyl hydrochloride in saline, cyamemazine in DMSO, and propericiazine in ethanol were added as concentrated solutions to the culture medium. Controls with DMSO alone or ethanol alone were done.

The phenothiazines alimemazine, cyamemazine and propericiazine as well as the anticholinergic drug trihexyphenidyl hydrochloride strongly inhibited, in a dose-dependent manner, the SMase activity of cultured human fibroblasts. No significant difference was found between the tested drugs. At 10μM, 60 to 70% inhibition was observed, and at 50μM, the SMase activity was reduced by 80 to 90%. By contrast, up to 100μM, lithium carbonate had no significant effect on the SMase activity. The SMase inhibition observed with a wide variety of drugs, exhibiting quite different pharmacological properties, is thus a non-specific effect which can be mainly ascribed to the amphiphilic characteristics of the drugs and not to their clinical activity.

References

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Sigma receptor characterized with (+)-[^{3}H]-3-(3-hydroxyphenyl)-N-(1-propyl)-piperidine on C6 glioma cells is a putative K^+ channel

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The existence of different opioid receptor subtypes has been described since many years. Among these, sigma site was thought to be responsible for psychotomimetic action of some opioid benzomorphans. More recently it has been shown that this site differs from the opiate receptor subtypes (no sensitivity to naloxone, reverse stereoselectivity for opiate benzomorphans) and differs from PCP receptor. Sigma receptor is also clearly different from D1- and D2-dopaminergic receptors.