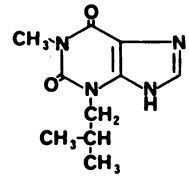
3-Isobutyl-1-methylxanthine

A potent phosphodiesterase inhibitor



IBMX

Adenosine-3',5'-cyclic monophosphate (cyclic AMP) has been implicated as a "second messenger," an intracellular regulator of hormonal action in the cells of various tissues.[1] A number of methylxanthines, for example, caffeine and theophylline, inhibit the activity of cyclic AMP phosphodiesterase (PDE), the enzyme which catalyzes the hydrolysis of cyclic AMP.

3-Isobutyl-1-methylxanthine (IBMX) was found to be a potent PDE inhibitor, about ten times as potent as theophylline in inhibiting cyclic AMP PDE.[2,3] **IBMX** inhibits cyclic nucleotide PDE with subsequent inhibition of cyclic nucleotide hydrolysis, resulting in accumulation of cyclic AMP and guanosine-3',5'-cyclic monophosphate (cyclic GMP).[4,5] An increase in cyclic AMP level results in activation of protein kinase[6] through which cyclic AMP is believed to act.

The potent inhibitory activity of **IBMX** has been of great importance in evaluating the role of the PDE system in regulating cyclic AMP levels.[7,8]

IBMX is finding increasing use as the antiphosphodiesterase agent of choice in studying cyclic AMP-dependent reactions. It has had great significance in studies of the problem of insulin-release control through inhibition of cyclic AMP PDE. **IBMX** reportedly stimulates insulin release by pancreatic islets when initiators of release, such as glucose, are present at appropriate concentrations.[3,9-11] In this context, studies of the surface changes on pancreatic β-cells following stimulation of insulin release have been performed.[12] It was also observed that PDE-inhibition-induced insulin release in the rat was more effective during pregnancy.[13]

Horrobin *et al.* reported that **IBMX** acted as an antagonist to prostaglandin E_1 in a perfused rat mesenteric preparation and suggested that prostaglandin antagonism may be a major action of methylxanthines.[14,15]

IBMX was found to stimulate the conversion of glycogen phosphorylase from the *a* to the *b* form in rat caudate nucleus slices.[16]

In studies on the relationship between cyclic AMP and allergic histamine release, it was found that **IBMX** markedly potentiated histamine release.[17,18]

It has been demonstrated that **IBMX** selectively inhibits cyclic GMP-associated PDE over PDE associated with cyclic AMP.[19,20]

IBMX has been used as an internal standard in the determination of theophylline by electron-capture GC.[21]

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