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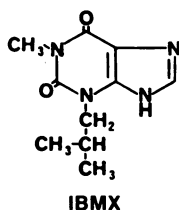
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A potent phosphodiesterase inhibitor



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 kinase⁶ 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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