ABSTRACT

It has been demonstrated that HMG is not only capable of decreasing total serum cholesterol but also decreases ester cholesterol, total esterified fatty acids and triglycerides of normocholesterolemic animals. HMG is effective both orally and intraperitoneally, the latter mode of administration appears more effective. The compound distinctly lowers the serum cholesterol content of cholesterolemic animals but fails to influence the liver cholesterol content of normal as well as cholesterolemic rats.

HMG also blocked the experimentally induced hypercholesterolemia both in serum and liver. It is readily absorbed when administered orally or intraperitoneally to the rats because lowering of serum cholesterol commences within 12 hours of HMG administration. The effect is maximum between 16–24 hours.
HMG is also capable of decreasing the serum total, ester cholesterol, total esterified fatty acids, phospholipids and triglycerides content of hyperlipemic rats to the extent of 35%, 46%, 33%, 19% and 50% respectively. On the basis of histological and histopathological studies of HMG-treated normocholesterolemic and hypercholesterolemic rats, it has been concluded that HMG has no toxic effects on the cellular architecture of liver, heart, kidney, adrenals, spleen, aorta, brain and lungs. Furthermore, administration of HMG to hypercholesterolemic rats causes quicker reversal of fatty liver changes towards normalcy. The appreciable increase in the hepatic reticuloendothelial cells of HMG-treated animals has been attributed to protective effect of HMG against hypercholesterolemia and fatty infiltration in liver.

In a preliminary pharmacological screening it has been found that HMG is completely inert and therefore it is superior to most of the known hypocholesterolemic and hypolipemic drugs which have harmful effects.

In cholesterol-fed rats, the hepatic HMG-CoA hydrolase (EC 3.1.2.5) activity is 3-5 fold increased. It has, therefore, been suggested that the rise in enzyme
activity is primary manifestation of cholesterol feeding; the secondary being the inhibition of HMG-CoA reductase (EC 1.1.1.34) activity by HMG released in vivo due to increase in HMG-CoA hydrolase activity.

On the basis of enzymic studies it has been hypothesized that cholesterol feed-back control might act by increasing the activity of HMG-CoA hydrolase, thereby increasing free HMG and decreasing cholesterol biosynthesis due to simple substrate analog competition.

On the basis of studies, so far made, it is concluded that HMG may be successfully used in the treatment of hypercholesterolemia and hyperlipemia provided in men the substance acts in the same way and is well tolerated.