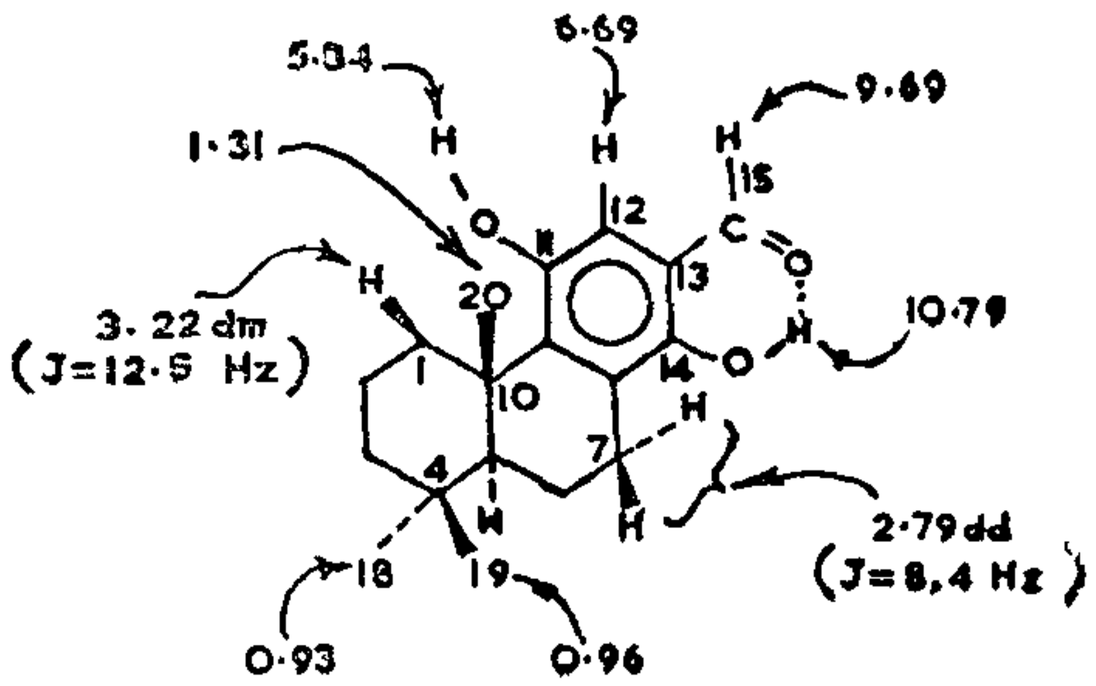
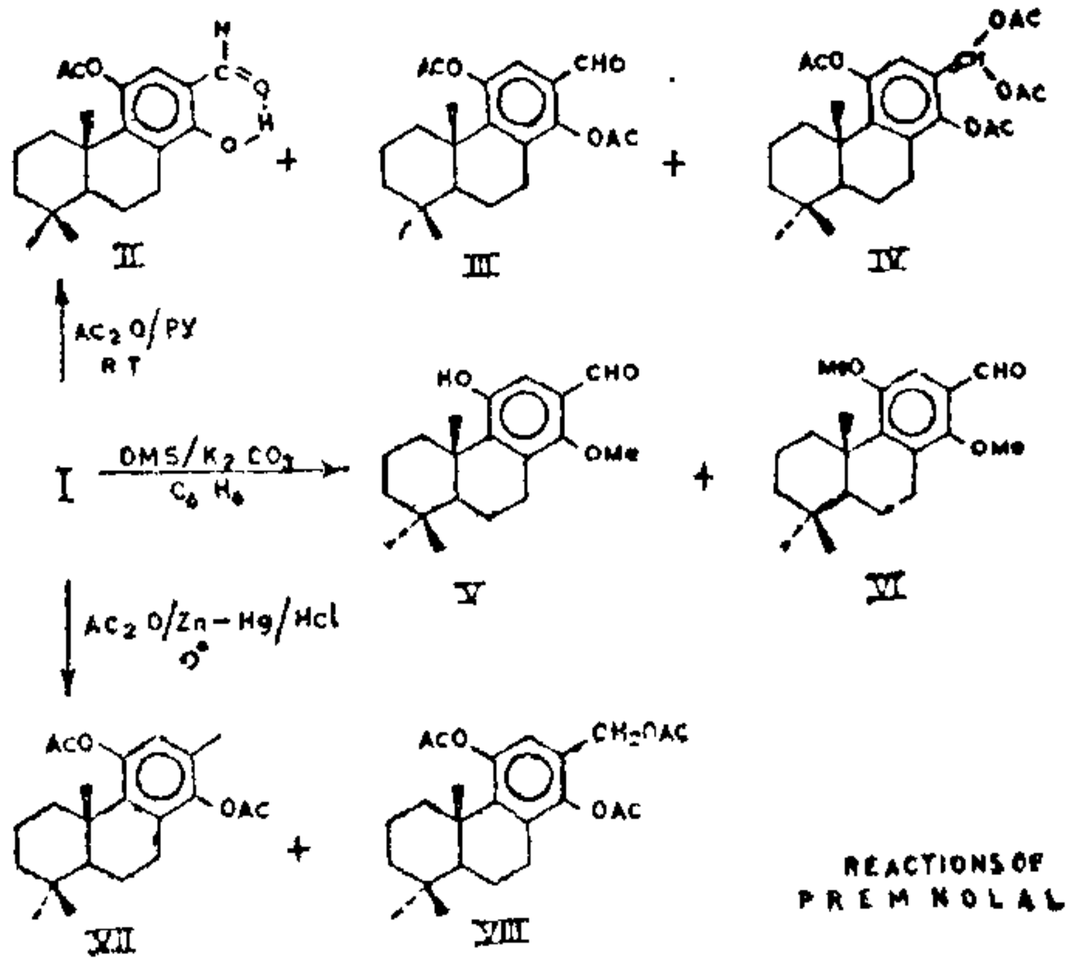
derivatives of abeitatriene of 5α: 10β normal configuration at the AB ring junction[4-8]. Thus premnolal can be represented as 13-formyl-11, 14-dihydroxy-podocarpa-8, 11, 13-triene (I).



I

Premnolal on acetylation using acetic anhydride saturated with dry hydrogen chloride in presence of zinc amalgam at 0° gave two acetates: premnol diacetate (VII), m.p. 132–132·5° ($C_{22}H_{30}O_4$) and 15-acetoxypremnol diacetate (VIII), liq. ($C_{24}H_{33}O_6$). VII was also prepared from premnolal by the sequence of reactions: reduction with sodium borohydride, tosylation, reduction using LAH followed by acetylation, and VIII by reduction with borohydride and acetylation. The structures of all the derivatives of I, assigned, are supported by their spectral data and analysis. The mass fragmentation pattern of premnolal (I) as well as premnol diacetate (VIII) agreed well with the results for aromatic diterpenes of podocarpa-8, 11 13-triene system published by Enzell *et al.*[1] and consistent with the structures assigned. The reactions of premnolal are summarised in the following chart.



Premnolal provides the first example of naturally occurring aromatic tricyclic diterpenes in which the isopropyl group is degraded to formyl in 13 position which might involve dealkylation and formylation or direct oxidative mechanism. Fuller details will be published elsewhere.

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LIPOGENIC ACTION OF CYCLIC AMP *IN VITRO*

BLECHER[1] observed a stimulatory action of high concentrations (10 mM) of dibutyril adenosine 3′, 5′ cyclic monophosphate on lipogenesis from glucose in fact cell suspensions *in vitro*. In contrast, an *in vitro* lipolytic action of exogenous adenosine 3′, 5′ cyclic monophosphate (cyclic AMP) had also been demonstrated[2]. I had noted lipogenic effect of cyclic AMP on the rat epididymal adipose tissue (EAT) segments *in vitro*. The results, along with the possibility of glycolytic kinases being a locus of lipogenic action of cyclic AMP *in vitro* are presented.

Results and Discussion

Details of experimental conditions for lipogenic studies and enzyme assays are described already[3]. In presence of 1 mM cyclic AMP, adipose tissue segments exhibited statistically significant higher (75% and 62%) lipogenic capacity (Fig. 1). 5′-adenosine monophosphate (5′ AMP) lacked such a stimulatory

effect. As low as 0·1 mM cyclic AMP could effectively stimulate lipogenesis (Fig. 2). Increasing the cyclic AMP concentration beyond 1 mM (which gave optimal stimulation) to 5 mM resulted in less stimulation. Again, 5′ AMP failed at all concentrations tested. The lipogenic effect of cyclic AMP was observable in presence of bovine serum albumin also.

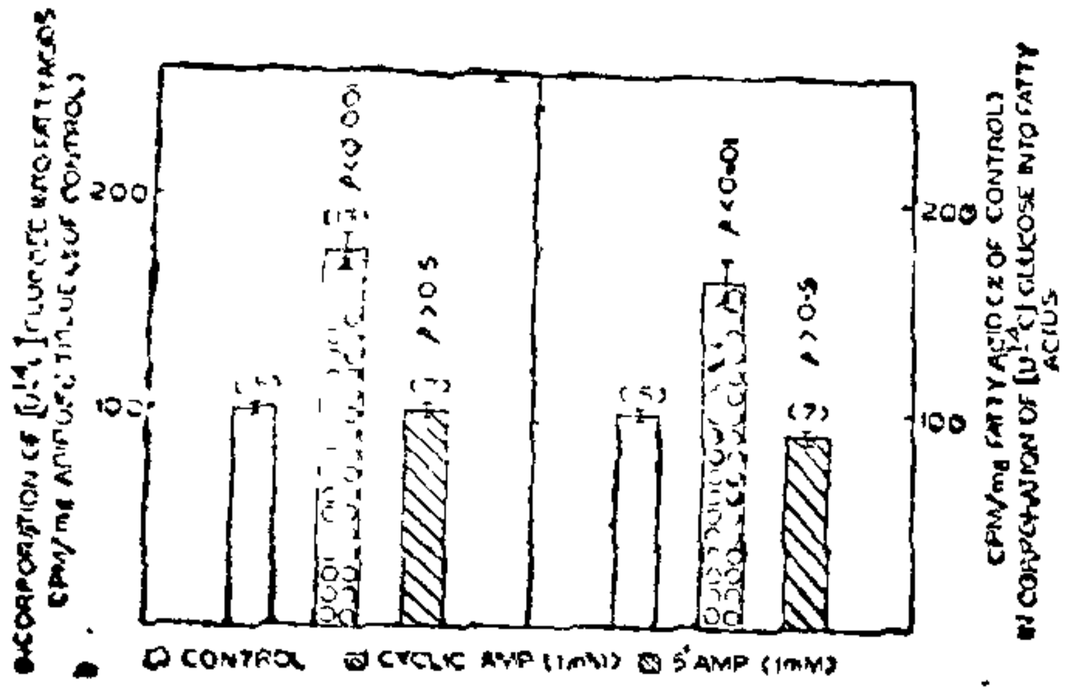

FIG. 1. Effect of cyclic AMP and 5′ AMP on the incorporation of (U–^{14}C) glucose in to fatty acids by male albino rat EAT *in vitro*.

50 mg adipose tissue segments were incubated in 1 ml of Krebs-Ringer Bicarbonate buffer, pH 7·4 containing 0·3 μ Ci of (U–^{14}C) glucose (2·77 μ moles) without or with 1 mM cyclic AMP or 1 mM 5′ AMP for 1 hr at 37° C. Control values were taken as 100 and the results expressed accordingly. Histograms show the mean and the bars S.E.M. Figures in parantheses represent number of observations.

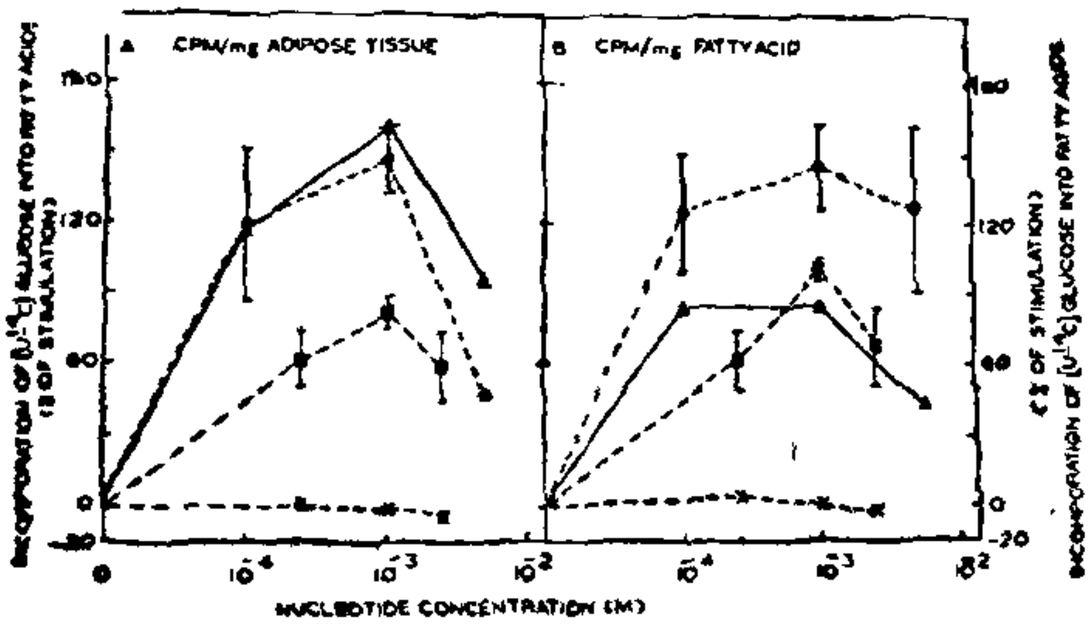

FIG. 2. Effect of different concentrations of cyclic AMP and 5′ AMP on lipogenesis.

Experimental conditions were the same as given under Fig. 1. Results shown as ■–– – –■ ▲———▲ and ●– – – –● represent effect of different concentrations of cyclic AMP in separate experiments, 1, 2 and 3 respectively. ×– – – –× represents lipogenesis measured in presence of different concentrations of 5′AMP.

The above results are in general agreement with previous reports about dibutyryl derivative of cyclic AMP[1,4]. It is known that adipose tissue phosphofructokinase can be activated by 2 micro moles per ml. of cyclic AMP[5] and this enzyme is a rate-regulating step in glycolysis[6]. Also, the nucleotide stimulated and inhibited glucose oxidation by dog thyroid homogenates at lower and higher doses respectively[7]. Perhaps a critical and narrow intracellular concentration range of cyclic AMP could bring about lipogenesis or lipolysis depending on its level[1,7]. However, the relative proportion of free (active) cyclic AMP to bound (reservoir) cyclic AMP[8], differential rates of glucose oxidation and re-esterification at various concentrations could also be important.

What is the mechanism by which cyclic AMP could stimulate lipogenesis? Cyclic AMP is known to influence the activities of many enzymes[5]. Since the conversion of glucose to fatty acids was the parameter measured, cyclic AMP could have activated hexokinase phosphofructokinase and pyruvatekinase the rate-regulatory enzymes of glycolysis. These enzymes are kinases of low activity and are almost irreversible. In preliminary experiments, 105,000 × g supernatants from EAT homogenates incubated with 1m M cyclic AMP for 10 min. at 37° had specific activities of 19·2, 14·8 and 71·7 when the kinases were assayed (controls: 8·7, 7·0 and 43·1 respectively). It is of interest to note that secondary sex tissues of rats injected with cyclic AMP have also exhibited higher activities of these kinases[11,10]. Cyclic AMP does not seem directly to influence the activities of hexokinase and pyruvatekinase. Cyclid AMP is known to bind and modulate the activity of phosphofurtokinase[12,13] the limiting enzyme in glycolysis. Stimulation of phosphofructokinase alone could result in the lowering of glucose-6-phosphate levels and elevation of fructose-1, 6-diphosphate levels, leading to higher activities of hexokinase and pyruvatekinase respectively. Hence, synchronised higher activities of the three kinases could lead to increased rate of glucose utilisation and provide a liberal supply of precursors for lipogenesis. Thus, a coherant "pull and push" mechanism may be operative, facilitating a faster rate of lipogenesis from glucose in cyclic AMP treated EAT segments *in vitro*.

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THE EFFECT OF VARYING THE POLARITY OF THE SOLVENT ON THE RATE OF CHLORINE-ADDITION TO OLEFINS

CHLORINE-addition to olefins in a moderately polar solvent such as acetic acid is an electrophilic reaction involving neutral molecules of olefin and chlorine as the reactive species[1]. The reaction is thus a typical example of a dipole-dipole reaction. The kinetics of this reaction in acetic acid has been recently investigated by adopting an experimental technique developed earlier in this laboratory for the chlorination of aromatic compounds[2,3]. The significant achievement in these investigations was the fact that the loss of chlorine due to volatility during a kinetic run was extremely low (less than 1%), an accuracy not achieved hitherto by earlier workers. Due to this new experimental technique, accurate kinetic and Arrhenius parameters could be evaluated. In this communication, the effect of increasing the polarity of the solvent (by the addition of water) on the rate of the reaction is reported. It is also shown that an empirical equation, first proposed by Seshadri and Ganesan[4] for a dipole-dipole reaction in solvents of varying polarity, is applicable in the present case.

The kinetics of chlorine-addition to butyl acrylate was studied in various acetic acid-water binary mixed solvents (water content being 0, 5, 10, 15, 20 and 25% by volume) at 26° C. For each solvent the second order rate constant (k_2) was evaluated by using the integrated rate equation

$$\log \{b(a-x)/a(b-x)\} = \{k_2(a-b)/2{\cdot}303\}\, t$$

as described in the earlier paper[2]. It was found that k_2 increased with increasing water-content (or dielectric constant) of the medium. This trend shows that the activated complex formed during the reaction is more polar than the reactants[5,6].

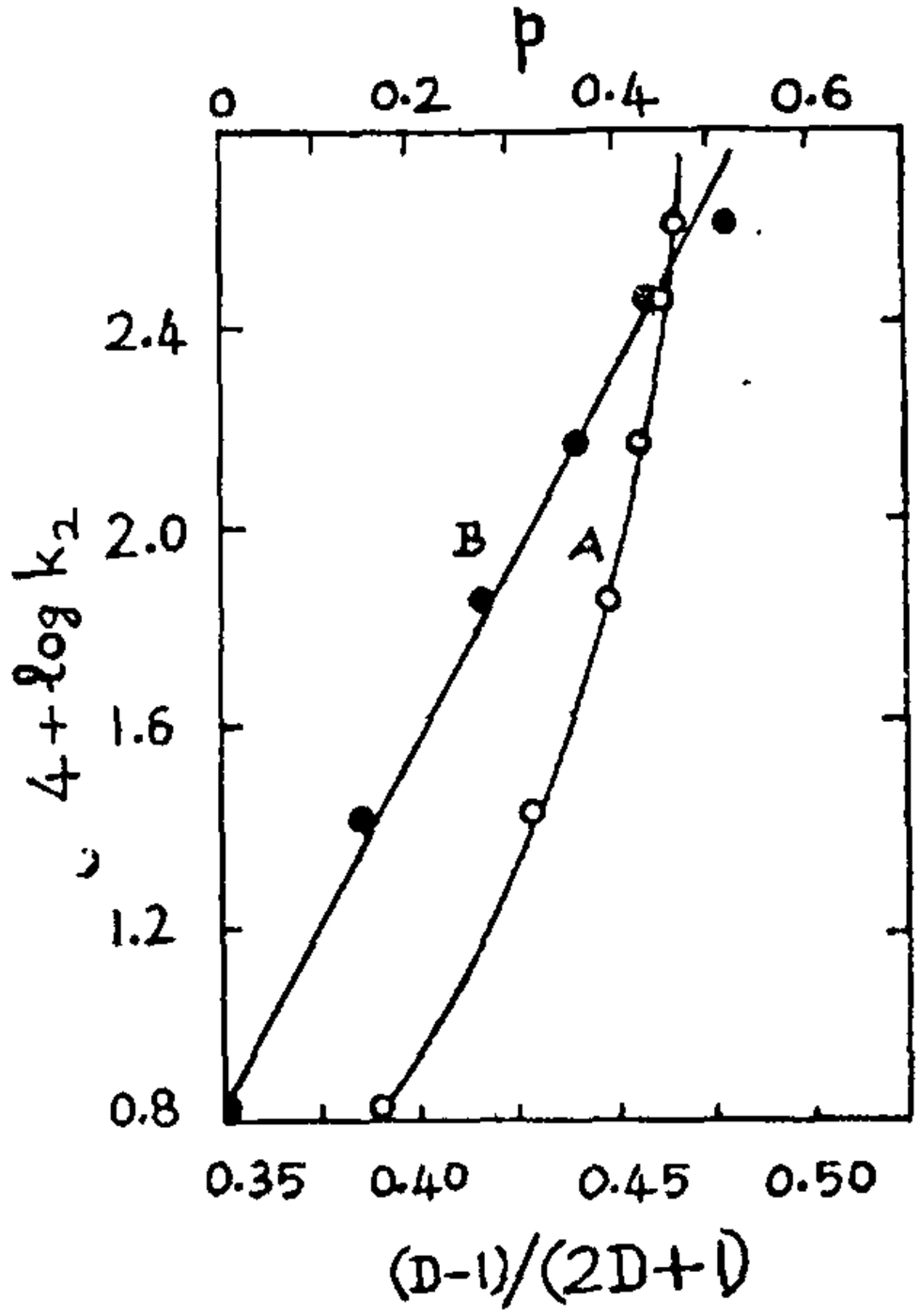

FIG. 1. Chlorine-addition to butyl acrylate in acetic acid-water mixed solvents at 26° C. A. Plot of log k_2 against $(D-1)/(2D+1)$. B. Plot of log k_2 against p.

Figure 1 shows plots connecting k_2 and the solvent properties. The plot of log k_2 against $(D-1)/(2D+1)$ is not linear (plot A), although it is expected to be so for a dipole-dipole reaction[7,8]. However, the limitations of such plots connecting the macroscopic dielectric constant (D) of the medium with the rate constant are very well known[9]. For a dipole-dipole reaction, such as the electrophilic bromination of paradimethoxy benzene in acetic acid-water mixtures, the following empirical equation was first proposed and found to be applicable[4],

$$k_{(aq)} = k_{(dry)}\, e^{ap}$$

A plot of log k against p was linear. Here $k_{(dry)}$ and $k_{(aq)}$ are the rate constants in dry and aqueous acetic acids, p is the mole fraction of water in the