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Alcoholic Liver Disease – The Possibility of Ayurvedic Therapy

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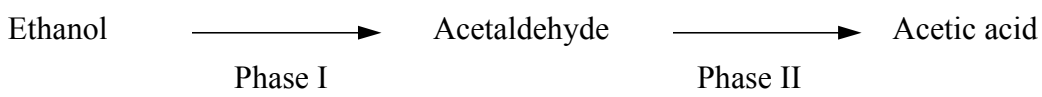
There is a general revival of interest in the alternative systems of medicine partly because of the inadequacies of the modern westernised systems of medicine and their hazards including the adverse reactions and the costs. Many traditional practices are being evaluated in the light of modern knowledge and understanding, but nothing worthwhile has been achieved. Ayurveda stands apart from the traditional practices and alternative medicine in that Ayurveda has a strong conceptual content and serious study of Ayurvedic concepts may lead to innovative research accelerating the progress of medicine along the proper lines (Kulkarni, 1986). Recent studies we have undertaken with ethanol metabolism strengthen the view that entirely new modes of action of drugs may be discovered, through the serious study of modern medical problems and Ayurvedic concepts.

The association between chronic alcoholism and serious liver disease including cirrhosis is well known (Holtzman *et al,* 1985). In France, the rationing of wine during the year 1941-1947 reduced the mortality from cirrhosis by 80 per cent. A relatively small consumption of alcohol acutely produces accumulation of lipids in the liver cells as a predictable and reversible pharmacological effect. However development of serious hepatic disease in chronic alcoholics is a complex problem. It is not clearly related to the quantity or the duration of consumption though these are important factors. Recent biochemical studies indicate that acetaldehyde formed as an intermediary metabolite of ethanol may be responsible for the liver damage associated with chronic alcoholism (Sorrel and Tuma, 1985).

Alcohol is mainly metabolised in the liver as follows:



Normally about 10 gm of ethanol are metabolised in one hour. In those who are chronic consumers of alcohol including social drinkers, the induction of enzymes involved in Phase I metabolism, especially in the gastrointestinal tract, results in a more rapid conversion of ethanol to acetaldehyde. Acetaldehyde is known to produce toxic effects on the liver cells and retard the rate of Phase II metabolism. This causes an accumulation of acetaldehyde which then leads to the formation of firm adducts with cell protein, resulting in cellular death (Liebev, 1988).

Acetaldehyde is normally formed during the body metabolism, especially from fats. Inadequate liver function reduces the capacity of the liver to metabolise acetaldehyde, which therefore tends to accumulate and produce several pharmacological effects. By its action on the central nervous system it causes anorexia. In fact the central nervous system appears to be particularly sensitive to this effect of acetaldehyde and may be playing a role in the regulation of a hunger-satiety rhythm. It is common knowledge that anorexia is the early and prominent symptom of liver disease. It has also been demonstrated that acetaldehyde specifically reduces the ability of the liver to synthesise albumin.

Chronic alcoholism is associated with anorexia and low serum albumin. It then becomes obvious that the key to prevention of alcoholic liver diseases lies in influencing acetaldehyde metabolism. But there is no known drug in modern medicine, which clinically influences acetaldehyde metabolism. Ayurveda does not specifically describe individual organ diseases neither are there specific remedies

for liver diseases. Liv.52, a proprietary Ayurvedic formulation, has been widely used in the treatment of liver diseases and the formulation contains ingredients described as having action of stimulating *agni* (appetite stimulant) and being a *rasayan* (protein anabolic)! Hence we decided to study the effect of Liv.52 on alcohol metabolism.

The main difficult in studying acetaldehyde metabolism was the lack of a reliable method of estimation of acetaldehyde in blood. The gas chromatographic method used so far was not free from artifacts. Fortunately Chauhan (1990) successfully devised modifications of the method to avoid the artifacts and established the reliability of estimation of acetaldehyde in blood and urine. Using this method we confirmed that, for the same amount of ethanol intake, chronic social users of alcohol have lower ethanol and higher acetaldehyde blood levels as compared to non-users of alcohol (Fig I).

FIGURE 1B

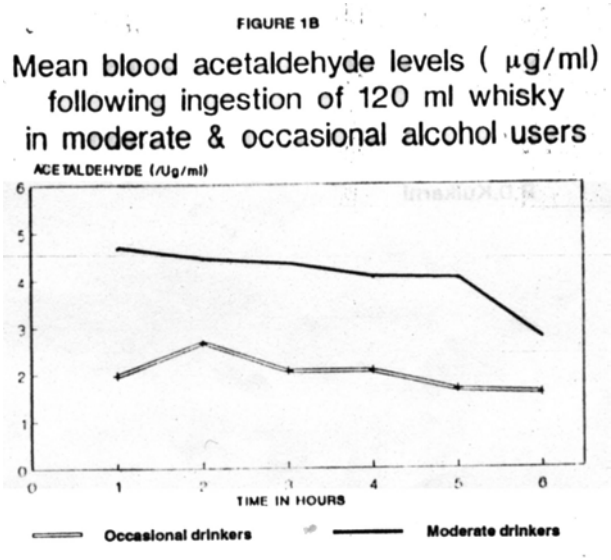
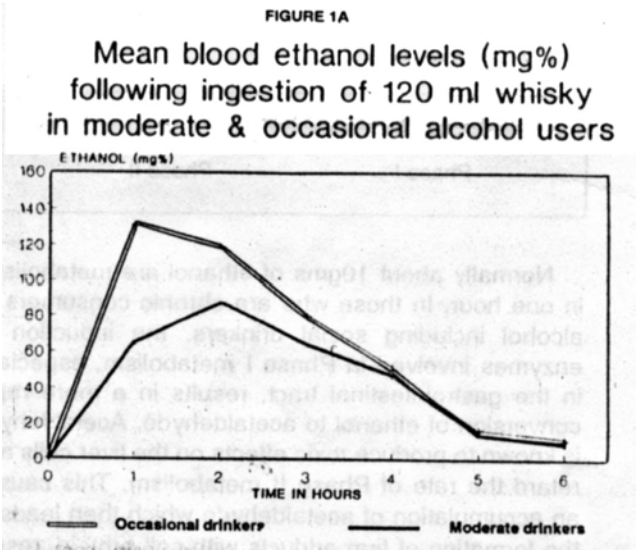
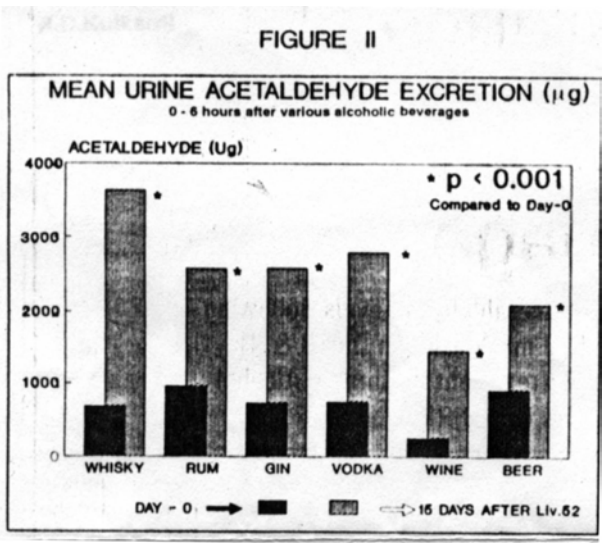


FIGURE 1A



Then we proceeded to study the effect of Liv.52 treatment on ethanol and acetaldehyde metabolism. Several chronic social users of alcohol with apparently normal liver function participated in this study. Blood alcohol and acetaldehyde levels were estimated after a fixed intake of alcohol in the form of whisky, before and after two weeks of treatment with Li.v52. We observed that treatment with Liv.52 caused increase in blood ethanol levels. The effect on the blood acetaldehyde levels however was complex. In the first hour after ingestion of alcohol there was an increase in acetaldehyde levels and subsequently rapid decline causing significantly lower blood acetaldehyde levels (Chauhan and Kulkarni, 1990). Subsequent studies showed that the rapid decline in blood acetaldehyde concentration was due to an increased excretion of acetaldehyde in urine. We repeated the experiments using different alcoholic beverages. Though the bioavailability of ethanol from different beverages varies, high acetaldehyde levels are seen with all of them and Liv.52 treatment enhances excretion of acetaldehyde in all cases (Fig. II).

FIGURE II



All the above results indicate two possible actions of Liv.52: (i) inhibition of intestinal enzymes responsible for enhanced metabolism and thus an increase in the bioavailability of ethanol and (ii) prevention of binding of acetaldehyde to cell proteins causing initial higher blood concentrations, and rapid excretion in the urine leading to a rapid decline in the blood levels.

This appears to be an interesting new concept. But this is not the first time that an Ayurvedic drug has been shown to have a mode of action unknown to modern medicine. A tranquillising action of drugs was known after observing the effects of Rauwolfia Serpertina on monkeys during its evaluation as an antihypertensive agent. If the binding of acetaldehyde to cell protein is responsible for irreversible liver damage, the prevention of this binding would be the appropriate way of preventing liver damage due to alcohol. Since a specific action has been demonstrated the way has been paved to develop a specific formulation of the prevention and treatment of alcoholic liver disease. It is also relevant to suggest at this stage that it is possible that alcoholic neuropathy and alcoholic cardiomyopathy (Korsten *et. al.*, 1978) may also be due to cellular accumulation of acetaldehyde and formulations can be developed to treat these conditions also.

'Scientists' often frown on the multiple ingredients in Ayurvedic formulation. This is a manifestation of ignorance of Ayurveda and a lack of perception of modern drug development. Ayurvedic pharmacy is a highly sophisticated discipline and formulations are aimed at enhancing the bioavailability of desired constituents, reducing the bioavailability of undesirable constituents, thus providing targeted delivery of the active principle to avoid unwanted widespread effects. Modern western medicine is still groping to achieve these objectives. In fact, modern medicine has learnt the hard way, that the so called "inert" substances in the single drug oral preparations are after all not so inert (Melikian *et. al.,* 1977).

Modern medicine has developed a scientific methodology to test concepts and hypotheses but lacks "a priori" conceptual base. Ayurveda has a powerful conceptual content but lacks easily available methodology to test it. Only the serious study and blend of both will lead innovative research and the rapid progress of safe therapeutics.

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