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THEORETICAL APPROACH TO LIFE PROCESSES
Part I. Propagation of the Processes by Water and Inhibition by Alcohol

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The role of water has been described in terms of a medium, propagating chain formation in life processes by virtue of an extensive hydrogen bond system. Alcohol also has a hydrogen bond system which could impart it a similar role. However, it does not have the solvent character nor transport capability to carry the vital ions required for the maintenance of cell equilibria. This is because of a reduction in the dielectric constant and capability for interaction with amino acids to form esters. It therefore, enters the living body as a toxic material and is biotransformed by the enzymic processes.

The mechanism of chain propagation and inhibition has been discussed in the light of the hypothesis on coordination polymer formation. It has been suggested that for assimilation the inputs of the living body should be hydrogen-bondable and they should not react unfavourably with the medium and/or the products of body reactions. Alcohol fulfils the first criterion and hence is easily assimilated. However, since it does not fulfil the second it has to be biodegraded. The bio-degradation process which proceeds through the alcohol dehydrogenase enzyme has been discussed with regard to the proposed mechanism.

Key words: Aging, Life process, Water, Alcohol.

INTRODUCTION

The role of water has been discussed earlier as a chain propagating medium in life processes by way of hydrogen bonding network. [1]. The water molecule in its tetrahedral structure form winds along the polypeptide helical chain [2] and promotes interaction through the hydrogen bonds created between the keto-imide and HOH linkages. Hydrogen bonding par excellence is thus the predominant feature of all living species.

Water acts as a transportation medium, it carries ions and molecules degraded or upgraded during life processes. Substances which enter a living body have to be hydrogen bondable in order to be assimilated by the system otherwise they are degraded by enzymic activities [3]. Such substances help life processes which do not disturb the hydrogen bonding super-structure. The reverse is also true i.e. substances which destroy the said structure are likely to prove toxic. Their toxicity would depend on how easily the toxicant and its metabolites are flushed out of the system. This paper is intended to discuss the effect of replacement of the hydronium ion in water by an ethyl group on the hydrogen bond super-structure.

It is known that ethanol is a toxic material which easily passes into the circulatory system and has a short life in the animal body. It is volatile and hence appears in the exhaled air immediately after ingestion [4]. Its aqueous solution, being non-volatile, is partially excreted by the urinary tract but it is largely chemically altered and hence the resultant metabolites are excreted by one of the several paths [5] of biotransformation.

The mechanism of interaction being suggested here is similar to that proposed earlier for tannage of hide powder and gelatin [6]. It was observed in the study that as the quantity of chromium increases, more cross linkages are introduced and the size of polymer units is reduced correspondingly. Chrome compound as presented to the pelt has chrome-ol bridges. For tannage the requirement is that the chrome-ol bridge should be hydrated and thus become hydrogen bondable. Water can induce the interaction of this type. The acidic conditions in which chrome tannage is carried out makes the carboxyl groups available for reaction with the newly opened chrome-ol bridge. A chrome-polypeptide bond is thus obtained [6].

In life processes tannage could be considered similar to attack of toxins to produce disease. If the bond can somehow be destabilized, detannage or detoxification would take place or, in other words, health would be restored. Water would be needed here to carry away the toxins from the bonding site. It is important that the water be of such quality as to help in the carrier process. For example, in case of chrome tannage the acidity conditions are critical and if the same is altered tannage would not take place. Similarly several mineral waters having therapeutic value act by introducing small or large ions to displace and leach out the toxins and residues from the tissues of the body. Detoxification is effected by the detannage mechanism using an appropriate aqueous solution or suspension of material of mineral or vegetable origin or a synthetic drug. An aqueous

medium is necessary in all cases for making substances available in hydrogen bondable form to render them assimilable.

Physical properties of water and alcohol with respect to the biological system. Water has the unique position among molecular liquids by virtue of its internal structure which comprises an extensive hydrogen bonded system. Physical properties of water are affected by hydrogen bonding to such an extent that they do not correspond to their analogues viz H_2S, H_2Se etc. It is tetrahedrally hydrogen bonded. It has an irregular tridymite like structure below 4° and irregular quartz like from 4° to 200°. It has a high dielectric constant and hence is considered a universal solvent. In the polypeptide chain it occupies a helical position.

Alcohol has the hydronium ion replaced by an ethyl group. Consequently the dielectric constant is reduced to 25.7. By virtue of the hydroxyl group, there is a hydrogen bonding system present but the same is not extensive. The result is that it cannot by itself form the helical chain along the peptides as done by water. In admixture with water the dielectric constant remains low indicating reduction of the extensive hydrogen bonded system to lower subunits or depolymerization of the water macromolecule.

Reaction of alcohol at different sites of a biological system. At the normal blood alcohol level of 0.03%, the body has the resorption capacity to abstract it from all its parts. In empty stomach it is absorbed within 40 minutes but in full stomachs the rate decreases. It has been estimated that 5% of the medium doses and 10% of high doses are elminated through lungs, skin and kidney while the remaining is oxidized in the body to carbon dioxide and water via acetaldehyde and acetate. An approximate equilibrium is reached one to one and a half hour after the ingestion of alcohol. Resorption from the gastro-intestinal canal is thereafter terminated. The alcohol level drops by approximately 0.15% per hour and it is suggested that an adult male transforms an average of 7g alcohol per hour and a female adult does 5.3g [4].

The specific pharmacological effect of alcohol is that in small doses it is a temporary stimulant and thereafter it is a depressant while large doses have a narcotic effect. Increase in blood pressure is noted after moderate doses due possibly to the constriction of splanchnic vessels and the heart beat increases. These changes constitute the stimulating effect of alcohol.

Small doses at a low level have very little effect on the polymeric structure of water and its dielectric constant is only very slightly altered. The metabolic process leading to the conversion to carbon dioxide perhaps imparts some warming effect. This together with the temporary increase in blood pressure is transmitted as the stimulant effect. However, this effect is short lived and as the level rises, the inhibitory effect becomes apparent. The water depolymerises and the extensive hydrogen bonding system is curtailed. The blood pressure decreases, the circulation is impaired, the vessels are dilated and the pulse slows down. The kidneys react with diuresis; they eliminate water and chlorides and the secretion of the gastro-intestinal canal is stimulated.

Alcohol increases the digestion of pepsin but an increase in its concentration inhibits fermentation mainly because the ferments are precipitated out [4].

The state of intoxication is determined from the alcohol level in blood. 0.03% is the normal physiological content of alcohol in blood, 1.0% is indicative of tipsiness, 1.5% is a sign of medium inebriation, 2.5% is heavy intoxication and 3.5% is a severe case of alcohol poisoning and could lead to death [4].

Biodegradation of alcohol. Most of the inputs for life processes are associated substances having macromolecular structure, involving hydrogen bonds. If unassociated, they should have hydrogen bondable groups. They are solubilized if the solute-solvent interaction is strong i.e. if the hydrogen bondable substance interacts favourably with water. The reaction of tannins which are otherwise only slightly soluble in water is effected with collagen by bringing the hydrogen bondable groups in the two species together. The reaction of importance here is that between tannins and collagen to produce vegetable tanned leather.

Alcohol has a high dielectric constant but much lower than water and is therefore a good solvent for associated or hydrogen bondable substances. It can form hydrogen bonds but the system is not extensive. With water itself it seems to have a strong solute-solvent interaction. It also forms strong complexes with hydrogen bondable substances and forms esters with acids. It reacts with amino acids generated during intensive reaction. The role of a carrier in life processes is consequently denied to alcohol. Change of the hydronium ion for an ethyl group thus brings about inhibition of life processes in contrast with water which promotes them. Alcohol therefore enters the biological system as a toxic material which adversely affects the subsequent enzymatic processes.

It may be stated here that alcohol ingestion is not ordinarily followed by an intake of water and hence, toxic effects of ethanol can not be diluted. In case the alcohol intake is small, the life process equilibria are not disturbed. These equilibria are struck between permanent fixation of the toxin into the polypeptide chain and the flushing effect whereby the tannage or fixation is retarded. In the former process cross-links are allowed and in the latter, they are reversed. This has been shown in the case of chrome tannage that acidity of the medium allows tannage otherwise there is no uptake of the metal by the proteinous system. Thus small concentrations of alcohol in the body system do not break the hydrogen bonding structure of water and the

protein but as the concentration rises the equilibrium is disturbed and the resorption becomes difficult. Under the circumstances ingested alcohol needs to be discarded by the metabolic processes.

Once absorbed by a biological system, different toxic materials, hydrogen bondable or otherwise, act differently. They may either be distributed into specific tissues or through a series of metabolic steps, may interact with multifunctional ligands such as proteins. The entering chemical may ultimately be bonded to one of the sites which has affinity for it or may be excreted by the kidney, respiratory tract or sweat glands. The chemical could also be altered through a biotransformation mechanism by specific or non-specific enzymes present in different organs [5].

It is important to know the role of ethanol and the possible effects it may have on the metabolism of drugs and other chemicals by chronic or acute ethanol ingestion. This information is all the more desireable in drug formulations which claim that ethanol has a potentiation effect on the latter.

It has been found that alcohol is metabolised to acetaldehyde and acetate and the latter is oxidized to CO_2. There is also a certain amount of alcohol left behind in the tissues, as residue. Hepatic alcohol dehydrogenase (ADH) enzyme is said to be responsible for the oxidation of ethanol to acetaldehyde. The reaction with ADH is catalysed as follows:

$$CH_3CHOH + NAD^+ = NADH + H^+ + CH_3CHO$$

The reaction requires NAD (nicotine adenine dinucleotide) which is reduced during the process of oxidation to acetaldehyde [7].

ADH contains zinc. Removal of zinc by dialysis or chemical reaction reduces/abolishes the enzymic activity [8]. Zinc compounds have only limited solubility in alcohol and hence any hydrolytic action on zinc linkages would tend to spilt off the metal compound.

Another important reaction during the metabolism of ethanol is the conversion of NAD^+ to $NADH_2$ which significantly decreases the $NAD^+/NADH_2$ ratio in liver. The shift of equilibrium thus obtained is critical for biochemical reactions and accounts for the metabolic effect observed in the case of ethanol.

The enzyme catalase and the microsomal oxidizing systems (MOS) are the other mechanisms for methanol and ethanol metabolism [7]. It has been reported that the microsomal oxidizing systems can oxidize both alcohols to their corresponding aldehydes and there is evidence that these metabolic paths depend upon the specificity of the various inducers and inhibitors.

There are conflicting evidences to show that stimulation of liver microsomal enzyme activity by several inducers does not necessarily increase the rate of alcohol metabolism. The evidences, however, do indicate that AHD is the major enzyme involved in the conversion of ethanol to acetaldehyde.

The conversion of acetaldehyde to acetate is carried out by aldehyde dehydrogenase which has a four to five fold larger activity in liver and kidney than ADH has. Acetaldehyde does not normally accumulate during the ethanol metabolism. Other liver enzymes are also capable of metabolising ethanol but their role has not been established. Both acute and chronic ethanol ingestion has an effect on lipid metabolism which results in the accumulation of lipid, primarily triglyceride in the liver. After ethanol ingestion the synthesis of triglyceride from fatty acid and glycerol has been shown to increase. Ethanol also decreases the rate of fatty acids oxidation by liver although the availability of acetate as a product of ethanol metabolism might depress the rate of fatty acid oxidation due to inhibition of other metabolic pathways. The effect of ethanol on fatty liver development is a complex series of biochemical events which are influenced by a variety of factors including dosage regimen, nutritional status etc.

CONCLUSION

As would be seen from the above discussion the ingestion of alcohol in doses that raise the blood level to higher than 0.03% has to take a different pathway similar to that of toxic materials. The difference appears in the form of lowering of the dielectric constant of water suggesting a decrease in the extent of hydrogen bonding. Such a medium is not ideal for the transport of essential ions. The living cells have to work at an optimum ionic concentration of Na, K, Ca and Mg and since their translocation becomes difficult, there is an inhibition of life processes which is indicative of aging.

Ingestion of alcohol demands extra work to be performed by the body: (i) for detoxification of the toxins of biotransformation, (ii) in getting the metabolites out of the system, (iii) in restoring the enzymic activity of liver and (iv) in restoring the hydrogen bonding super structure of the body. Alcohol consumption therefore inhibits life processes or ages the body in more than one way.

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