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Studies to utilize physicochemical methods for the regeneration of potential foods during space missions of long duration are in progress. It was decided that synthesis of carbohydrates or carbohydrate-like materials such as formose sugars and glycerol offered the greatest promise. Starting materials would be metabolically produced carbon dioxide and water. Hydrogen obtained as a byproduct from the electrolysis of water in the oxygen recovery system reacts with carbon dioxide to produce methane

which is oxidized to formaldehyde. A prototype apparatus which accomplishes this conversion has been constructed and is in operation. The formaldehyde is converted to formose sugars or alternately to trioses which are catalytically reduced to glycerol. A continuous flow reactor capable of producing 750 g per hr of formose sugars is in operation. Since all the reactions except the electrolysis to yield hydrogen and oxygen are exothermic, energy requirements are minimal.

As is evident from the subject of this symposium, chemically synthesized substances are used extensively in the food industry. However, the proportion of such materials incorporated into food is usually quite minor and only sufficient to accomplish its intended purpose, whether it be to add nutritive value, as for example certain amino acids and vitamins, or to confer desirable flavor, aroma, texture, or resistance to microbial attack.

In this paper, a quite different rationale for the incorporation of synthetic substances into food will be discussed. This arises from the logistic requirements of long duration space missions where the food supply could comprise a significant fraction of the total payload. Thus, if pure synthetic nutrients could be recovered from waste and utilized as food by the crew, considerable savings in weight and volume might result (Drake *et al.*, 1966; Jagow and Thomas, 1966; NASA, 1967). For such a system to be economical, it is necessary that the regenerative systems be simple, efficient, and highly reliable. Therefore, it is almost essential that the crew be able to consume safely each regenerated pure nutrient as a significant part of the diet (Shapira, 1967).

There are a number of potential pure nutrients which might be suitable for the aerospace situation. This discussion will be limited to only two of these—glycerol and formose sugars—and the current effort toward the development of a system which would regenerate them from carbon dioxide and water.

NUTRITIVE VALUE OF GLYCEROL

Man normally consumes 10 to 40 g per day of glycerol as a component of dietary lipids. It usually comprises less than 5 to 10% of dietary calories. The first intentional use of pure glycerol in man as food was reported by Ferber and Rabinowitsch (1929). Of the 60 subjects consuming glycerol, 100 g of glycerol in solution as a single dose increased blood sugar, and only five subjects complained of any discomfort. Fourteen young human subjects were able to ingest 110 g per day of pure glycerol for 50 days without difficulty or obvious detrimental effect (Johnson *et al.*, 1933). This quantity of glycerol provided approximately 20% of the caloric requirements. In the same study, normal growth of rats occurred over a period of 40 weeks, when glycerol constituted 41% by weight of the diet; normal growth occurred in dogs fed a diet containing 35% by weight glycerol for 50 weeks. In an acute situation, a 2¹/₂-year-old child consumed 300 g of glycerol orally (23 gm/Kg) and survived (Thomas, 1963).

In recent years, orally administered glycerol has been employed extensively for its therapeutic value in increased ocular and intracranial pressure, and to a lesser degree in the treatment of diabetes. Based upon the initial studies of Cantore *et al.* (1964), oral glycerol has been used in cases of increased intracranial pressure. It was reported that patients with "pseudotumor cerebri" were given 0.5 g per kg per day for 8 weeks and "found to be fairly well tolerated." When 85 to 280 g per day were consumed for many weeks by patients with raised intracranial pressure, no toxic effects were noted (Buckell and Walsh, 1964). With a 7-year-old boy consuming 3 g per kg per day for 126 days (as long as the case was followed), there was improvement of benign intracranial hypertension with reduction of papilloedema and no mention of undesirable side effects of the glycerol (Absolon, 1966). Glycerol has even been administered with favorable results in newborn infants at the rate of 3.75 g per kg in 50 cases of cerebral injury (Polleri, 1965).

Extensive therapeutic use of glycerol for glaucoma and other eye diseases started with the report of Thomas (1963). In these situations, the beneficial effect is probably due to a blood-tissue osmotic interaction where water is removed from the tissue. At least 50 publications have appeared describing situations in which glycerol was administered for its therapeutic effects without mention of side effects (Shapira, 1968). These studies have shown that divided doses of 300 g per day (over 1300 Kcal/day) of glycerol for extended periods are well tolerated by man. These amounts on a per kg basis are considerably lower than what has been shown to be toxic in animals. In fact, orally administered glycerol appears to be less acutely toxic than glucose (Spector, 1956).

Glycerol is rapidly and almost completely converted into glucose by the body unless the renal threshold is exceeded (Gidez and Karnovsky, 1954; Hagon, 1953). Various studies have been conducted to determine the rate of this conversion in both normal and diabetic subjects (Freund, 1968) and also in working and resting individuals (Young *et al.*, 1967).

It will be necessary for the crew to consume the glycerol in regulated amounts during the course of the day. This may not be particularly unpleasant, because dilute glycerol solutions are fairly sweet and when flavored appropriately, for example with lemon or lime juice, are almost indistinguishable from flavored sugar solutions. Further, the glycerol can be used as sweetening for coffee and tea. It is even possible, by the addition of small amounts of natural gums, to produce acceptable semi-soft and hard candies.

On the basis of animal feeding studies, it is known that diets

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containing 40% glycerol are well tolerated (Shapira, 1968). However, it is unlikely that the crew will be expected to consume this much material. Glycerol as 20 to 30% of the diet is within reason and might result in a significant reduction in weight and volume of stored food for long duration missions if a suitable regenerative system for its synthesis can be developed.

NUTRITIVE VALUE OF FORMOSE SUGARS

There are few reports in the literature concerning the nutritive qualities of formose sugars obtained from the self-condensation of formaldehyde. One would expect the results to be quite variable, depending upon the method of preparation and the exact composition of the mixture. Most formose mixtures contain a wide variety of sugars whose individual metabolism is not well defined. Further, the sugars exist as racemic mixtures and the available evidence indicates that the unnatural enantiomorph is poorly utilized, if at all.

Ewart (1925) reported that mixed adventitious microorganisms utilized formose sugars for growth, but sugars which were primarily pentoses remained which could not be metabolized.

With *Saccharomyces cerevisiae*, a batch prepared sample of formose was only 4.5% as effective as D-glucose as a carbon source for growth (Akerlof and Mitchell, 1964). When a similar test was made with *Saccharomyces carlsbergensis* utilizing a sample from a continuous reactor, 20 to 25% of the growth resulting with D-glucose was obtained. Although it is difficult to explain, it was concluded that about half this latter formose mixture was comprised of glucose, fructose, and mannose.

When formose sugars were fed to rats (Akerlof and Mitchell, 1964) in the range of 30 to 50% of the diet, the animals consumed less food, lost weight, developed diarrhea, and eventually died. Three major fractions of the formose mixture obtained by chromatography on cellulose were all toxic. It was concluded that most, if not all, the toxicity was due to formaldehyde present as the hemiacetal derivative of the sugars. The possibility that formaldehyde produced the toxic effects has been examined further (Shapira, 1968). When formose sugars completely freed of formaldehyde were fed to rats as 40% of the diet, the animals suffered the same symptomatology as observed previously, although they did survive somewhat longer. Addition of 1.6% paraformaldehyde to control diets containing glucose did not produce the effects noted with formose. It appears that the toxicity is not due to formaldehyde, but rather to a specific carbohydrate component or components of the mixture.

The formose mixture contains equimolar amounts of all stereoisomers, including the nonphysiological L-isomers of the common sugars in the diet. The L-isomers might be the cause of the observed toxicity, but the limited literature that exists does not seem to bear this out. For example, L-glucose could not be oxidized by *Escherichia coli*, *Bacillus aerogenes*, nor surviving slices of rat brain and Sarcoma 39 tissues (Rudney, 1940). It did not interfere with the oxidation of D-glucose in these systems. Brewer's yeast does not ferment L-glucose (Fischer, 1890). When L-glucose is injected into rats at high levels, almost all is recovered unchanged in the urine (Rudney, 1940).

Fortunately, it may be possible to separate metabolizable D-hexoses from the reaction mixture and return the other sugars to the reactor to reequilibrate. If a suitable enzyme such as hexokinase could be stabilized and convert selected sugars in the mixture into their phosphate derivatives, ion

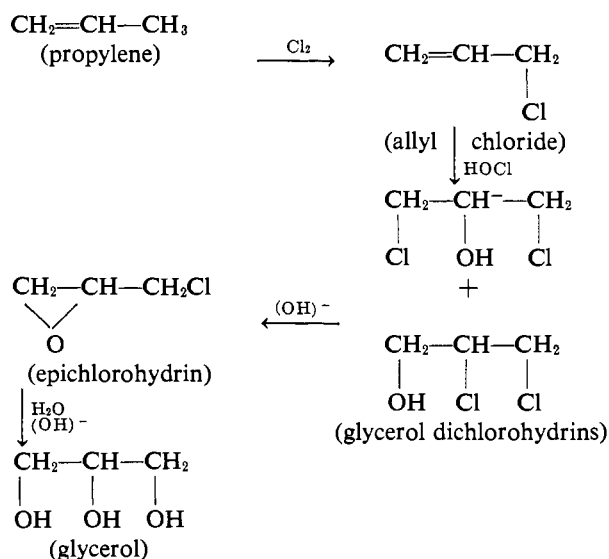
exchange methods could be used to separate the hexose phosphates from the neutral unreacted sugars. A system for regenerating ATP from ADP would also be required. Efforts to accomplish these reactions are in progress.

POTENTIAL SYSTEMS FOR THE SYNTHESIS OF GLYCEROL

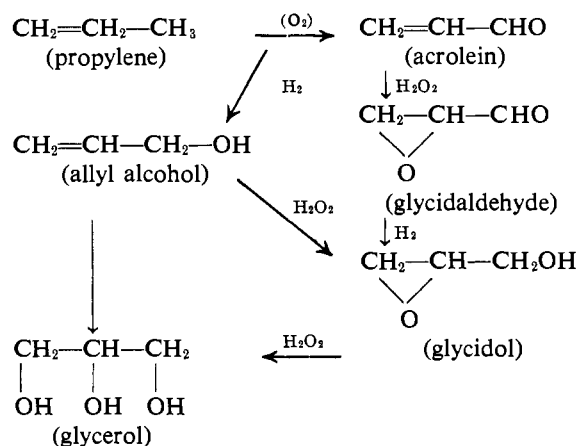
Assuming the availability of carbon dioxide and water as raw materials, a considerable number of possible routes for the synthesis of glycerol are possible. The choice between them will be dictated by weight-power-volume-reliability considerations.

One might first consider the commercial synthetic processes currently used to produce more than one-half the glycerol manufactured. The remainder is obtained as a byproduct of the soap industry.

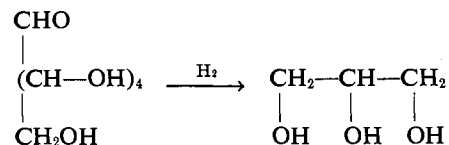
In most synthetic processes, propylene is used as a starting material. The most commonly used reactions which involve allyl chloride as an intermediate are:



Alternative processes are based upon conversion of propylene to acrolein. The reactions are:



Finally, appreciable amounts of glycerol are made by the reductive splitting of sugars. For example, with a hexose, the reaction is:



glycolaldehyde and then a series of Aldol condensations. A neutral or slightly alkaline pH is required for the reaction.

A wide variety of compounds are able to catalyze the reaction. Aside from the most commonly used catalyst, calcium hydroxide, all of the alkaline earth oxides and hydroxides have been shown to be more or less active. There have been reports concerning the use of lead, copper, zinc, and iron oxides as catalysts (Shapira, 1967).

The Cannizzaro reaction which results in disproportionation of formaldehyde to methanol and formic acid and, to a lesser degree, causes changes in the products of the reaction must be minimized. The relative rates of the various simultaneous reactions that occur in the reaction mixture can be controlled by adjustment of parameters such as alkalinity, temperature, and catalyst. Catalysts serve two major roles (Pfeil and Ruckert, 1961). First, some affect the lag period of initial condensation which produces glycolaldehyde. Various homogeneous and heterogeneous catalysts are able to reduce the lag period by a large factor. Second, other catalysts, including the products of the reaction, are able to alter the rate of the subsequent Aldol condensations and cause the autocatalytic effects observed.

The kinetics of the reaction have been the subject of recent reports. It was found that below 80% conversion of formaldehyde in a homogeneous system, the major products were glycolaldehyde, trioses, and tetroses, each of which is a catalyst and reactant (Weiss and Shapira, 1968). It was possible to correlate their rate of production by the expression

$$d(A_2 + A_3 + A_4)dt = 0.0582(A_1 + A_2 + A_3 + A_4) \times (A_2 + A_3 + A_4)Ca(OH)_2$$

where A_m is the concentration of species of carbon number m , concentrations are molar, and time is in minutes.

This concept of the kinetics was later refined by making the assumption that the rate expressions for the reaction which occurs in homogeneous solutions were analogous to Langmuir-Hinshelwood relationships for adsorption and desorption in heterogeneous systems, since complexing and decomplexing of the catalyst were rate limiting (Weiss *et al.*, 1970).

The detailed mechanism by which the higher sugars arise is not known. The three-carbon compounds, glyceraldehyde and dihydroxyacetone, which are produced immediately after glycolaldehyde must arise from an Aldol condensation glycolaldehyde with formaldehyde (Fischer and Tefel, 1887). Several schemes have been proposed for the further reactions (Langenbeck *et al.*, 1956), including one which requires the branched chain hexose, dendrokotose, as an essential intermediate (Katzschmann, 1944).

DEVELOPMENT OF A SYSTEM FOR CONVERSION OF CARBON DIOXIDE TO FORMALDEHYDE

The reaction sequence involving methane oxidation was chosen for investigation because it operates at atmospheric pressure which obviates the need for heavy reactors and compressors, it occurs in the gas phase using solid and/or gaseous catalysts, and the byproducts of the reaction should be easily separated.

The problem of converting carbon dioxide into formaldehyde is being investigated (Budininkas *et al.*, 1968). First, a prototype system was developed which utilized methane in the feed. The reactor consisted of a vertical Vycor glass 28-mm-i.d. tube containing a 100-mm long heated zone filled with approximately 40 cc of porcelain Berl saddles coated with alkali tetraborate. The effluent gas was passed

through traps where formaldehyde and water were condensed. A portion of the residual gases was vented to permit addition of fresh feed gases which were methane, oxygen, air, and nitric oxide.

Experiments were conducted normally at 678° C and a recycle gas velocity of 5000 cc per minute. Recycle ratio was varied. Nitric oxide was maintained at 0.2%. The composition of the recycling gas was controlled by adjusting the flow rates of the individual feed gases. A material balance could be obtained from the yield of formaldehyde, the flow rates, and vent gas analysis for CH₄, O₂, CO, and CO₂.

It was found that when methane was present as 15 to 30% of the gas mixture the total formaldehyde yield increased with the recycle ratio. However, the yield per pass decreased with an increase in the recycle ratio and appeared to reach an asymptotic limiting value of 0.9 to 1.0% per pass.

A series of tests were conducted at a recycle ratio of 25. The optimum concentration of methane was 30%, whereas variation of the oxygen concentration between 5 and 15% did not influence the yield of formaldehyde. However, when the concentration of oxygen was increased beyond 8 to 9%, the amount of byproduct carbon dioxide formed increased considerably. The best utilization of reactants was obtained with a recycle gas containing 29% CH₄ and 7% O₂ by volume. The average formaldehyde yield was 27%; an additional 17% of the methane was converted to CO and 6.5% to CO₂.

Later, the system was modified to incorporate a heat exchanger and a second loop which contained a Sabatier reactor. The system is completely closed and operated to convert CO₂, H₂, and O₂ into only formaldehyde and water. Since the oxidation reaction is exothermic, no external heating would be needed in theory. In practice, small amounts of electrical energy are needed to compensate for insulation losses and heat-exchanger inefficiency.

DEVELOPMENT OF A SYSTEM FOR CONVERSION OF FORMALDEHYDE INTO GLYCEROL

It should be possible to control the self-condensation of formaldehyde to predominantly glyceraldehyde and dihydroxyacetone, which in turn should be readily reduced to glycerol. Other possible schemes for the synthesis of glycerol from carbon dioxide can be postulated but all of these involve a more complex sequence of reactions.

There are several reports in the literature describing methods for the control of the formaldehyde condensation to produce trioses. As early as 1906, it was observed that heating 2% aqueous formaldehyde with calcium carbonate yielded primarily trioses (Euler and Euler, 1906; Leow, 1906). Zinc carbonate, sodium sulfite, and magnesium oxide also cause a similar conversion of formaldehyde to trioses (Leob, 1909; Seywetz and Gibello, 1904; Binko and Kilar, 1959). Several other more complicated schemes for converting formaldehyde to trioses have been reported and reviewed (Binko and Kilar, 1959).

All of the preceding methods involve the use of homogeneous catalysts. For spacecraft application, a heterogeneous catalyst would be much preferred and efforts were made to develop one. A number of alumina-based catalysts to which were added 20% CaO, Fe₂O₃, and PbO were tested in a heterogeneous flow reactor for their ability to produce formose sugars from formaldehyde (Weiss *et al.*, 1969). With 5% glucose added to the reactants as a cocatalyst, there was about 39% conversion to trioses with the CaO-Al₂O₃ catalyst. Under the same conditions with 5% glyceraldehyde as the

cocatalyst, there was 71% total conversion, with trioses comprising 73% of the product. The yield of trioses was not solely dependent upon total conversion since with a PbO-Al₂O₃ catalyst there was 40% conversion, of which 42% was trioses, 16% tetroses, 13% pentoses, and 29% hexoses.

Reduction with hydrogen of trioses to glycerol may require special catalysts (Weiss *et al.*, 1969). A mixed Raney nickel-platinum oxide catalyst was effective, but the product glycerol effectively complexed with and dissolved the nickel in the catalyst mixture. A 5% ruthenium on carbon catalyst gave an initial rate of 1.7×10^{-2} moles per hr per g catalyst which was more than adequate for the intended use.

DEVELOPMENT OF A SYSTEM FOR THE SYNTHESIS OF FORMOSE SUGARS

Virtually all of the studies of the formation of formose sugars have involved batch reactions. For aerospace application, a continuous process is more desirable. Such a system was first developed by Akerlof and Mitchell (1964). A reaction mixture of 1.5M formaldehyde and 0.15M calcium hydroxide was passed through a 5-m coil having a 3-mm i.d. held at 60° at the rate of 4 ml per min (residence time was 8.5 min). The effluent was treated with carbon dioxide, filtered, deionized, and concentrated under reduced pressure, and yielded about 7.5 g per hr of formose sugars. Subsequently, the apparatus and conditions were modified (Shapira, 1968) to permit the synthesis of about 110 g per hr of formose.

A plug flow apparatus suffers from the fact that the reaction cannot be easily controlled and the product is more complex than one which would arise if the reaction did not go to completion. This problem can be solved by the use of a continuous back-mix reactor (Weiss and Shapira, 1968; Weiss *et al.*, 1970). A further advantage of this type of reactor is that much larger quantities of materials can be processed in a small reactor with good control of the conditions. A 500-ml back-mix reactor can produce more than 1 kg per hr of formose. Since at low conversion levels a much simpler mixture of sugars is produced, it is possible that a high proportion may be metabolically useful.

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