APPROACHES TO THE CHEMICAL SYNTHESIS OF FOOD[1]

Cat 04

J. SHAPIRA

ABSTRACT

N 68-27463

The conversion of human metabolic products such as carbon dioxide, water, and urea into materials which might be used as food during extended space missions has been of concern to the NASA for some time. A relatively new approach to this problem is to synthesize by purely chemical methods compounds which would satisfy a major portion of the astronaut's calorie requirements. Formose sugars, which can be readily prepared from formaldehyde, represent one such potential food. Unfortunately, crude as well as partially purified formose is toxic to weanling rats when fed at high levels. This toxicity may be due to materials which can be eliminated by proper modification of the catalyst, reaction conditions, or methods of purification. An alternative chemically synthesized food is represented by glycerol and some of its derivatives. In this case, there has been much greater success in feeding studies. Individually up to 40% by weight of some of these compounds was compatible with good growth. An even higher total concentration of certain combinations of these low molecular weight materials was tolerated. The feasibility of actually synthesizing these compounds in the space environment has been explored. The implications of these studies as related to the predicted shortage of food in the world should not be ignored.

---

[1] Manuscript received__________. Contribution from the Biotechnology Division, Ames Research Center, NASA, Moffett Field, California 94035. The views expressed by the author are solely his own and should not be interpreted to represent an official position of the NASA. Presented at 52nd Annual Meeting, Los Angeles, California, April 1967.

[redacted]

TMX-59839
Code 1
Page 22

[redacted]

CFSTI H.C. 3.00
" MF .65

One of the approaches under investigation at the NASA, Ames Research Center for providing food for astronauts during extended space missions is to synthesize materials by chemical methods from carbon dioxide, water, and urea which could be incorporated into the diet.

The studies reported here are but one aspect of the greater problem of providing a "closed ecological system" during these missions and thus regenerating, as much as possible, those components required for life support. Considerable progress has been made in the recovery of water from urine and the cabin atmosphere, and of oxygen by electrolysis of recovered water. Unfortunately, the recovery of carbon as food has presented considerably greater difficulty. Efforts have been made to utilize algae, microorganisms, duckweed, etc., for the conversion of carbon dioxide to food materials. It has even been suggested that these materials might serve as food for higher life forms which would in turn provide more conventional food for the astronauts. The research along these lines has recently been summarized (1). It has been concluded (2,3) that these approaches have a potential usefulness but that the practical problems related to their application are great. For example, if light must be generated on-board for the growth of a photosynthetic organism such as algae, large losses of energy are incurred in the conversion of electricity to light and the resultant heat requires the presence of a complex system for its dissipation into space. In addition, algae have not yet been sufficiently purified to produce food which can be fed at high levels for prolonged periods. Microorganisms as a major component of the diet present other problems. The high protein and nucleic acid content of this material would require a very much increased rate of water ingestion and excretion to clear nitrogen from the body. Aside from the problems in logistics this raises, it can be questioned as to what effect this chronic overload on body organs such as the liver and kidney will have. Accordingly, an effort was begun early in 1966 to explore the possibility of using chemically synthesized materials as food.

Considerations Involved

The rationale for the approach involving low molecular weight organic compounds as food has been reported (4). In summary, the considerations were these:

(1) Thermodynamically, the amount of energy needed to combine carbon dioxide and water to give compounds with greater energy content is independent of the process involved. In practice, certain losses are incurred which reduce the efficiency. Calculations, based upon assumptions which have not yet been tested, can be made to show that the most efficient process may be one involving straightforward chemical reactions similar to those accomplished today in chemical plants throughout the world.

(2) The use of chemical processes may reduce requirements for volume and weight below that required for other regenerative processes.

(3) It is known that low molecular weight organic compounds derived from food are metabolized in large amounts by the body. It has also been shown that many of these, for example, glyceraldehyde (5,6,7), dihydroxyacetone (8,9,10), and glycerol (11), are readily metabolized by the body when ingested in small amounts.

(4) The major portion of our diet supplies only calories for body activity and maintenance. Relatively simple materials such as glucose are known to be able to satisfy this requirement. The recognized essential components of the diet include approximately 35 g/day of protein (or a significantly smaller amount of the essential amino acids), 2-5 g/day of polyunsaturated

fat, 5-10 g/day of salts, trace elements and vitamins, and perhaps a minimal amount of conventional carbohydrate. In all, these essential components account for less than 10% by weight of food and the remainder of the food is used by the body for its calorie content.

Limitations of the Approach

It is well recognized by those who are concerned with planning for space missions of long duration that a "normal diet" is the most desirable method for providing food for the crew. However, even with present relatively short missions, dehydrated food is used because of considerations such as ease of storage and stability. At some point of mission size, duration, and complexity, the possibility of providing at least a portion of the food as materials regenerated during flight can be shown to be very advantageous (2). Of course, any such regenerated food must satisfy the criteria of any food, that is, be nutritionally adequate, acceptable, and safe to consume for extended periods.

Thus, it is postulated here that on missions of very long duration, the essential components of the diet will be carried along but that as much as possible of the astronaut's calorie requirements will be supplied as simple regenerated organic compounds.

There are several major restraints on the possible compounds. They must:

(1) Be safe and acceptable foods under the circumstances in which they will be used. Although there is no data to suggest that the conditions of weightlessness, confinement, and inactivity require special dietary considerations, adoption of a novel food will require studies under these conditions before its use in extended missions.

(2) Be readily synthesized under space flight conditions with high reliability and minimum operational and maintenance requirements. The scope and complexity of chemical substances which can likely be synthesized during space flight are limited.

(3) Provide a significant proportion of the total calorie requirement. There would be little or no advantage if a considerable number of different compounds had to be synthesized or a compound required in only small amounts, e.g., a vitamin, were synthesized.

(4) Result in a major advantage with regard to weight, volume, or power requirements over the total duration of the mission. For one possible chemical food, glycerol, calculations have been made (2) for the potential savings. Assuming that glycerol meets all the criteria as food, there would be about a 25% saving in food weight for a 400-day mission to Mars with a crew of 10 men if 50% of the diet were regenerated glycerol. The saving becomes much greater with longer mission durations.

It is recognized that a realistic program to investigate the use of chemically synthesized materials as food is inherently a prolonged one involving generations of animals. At the present time, the effort is being concentrated on two basic aspects of the problem.

(1) What simple organic compounds can safely be incorporated into the diets of animals in large amounts?

(2) What simple organic compounds can possibly be synthesized efficiently within the restraints imposed by space flight?

Formose Sugars

The first material investigated here for its potential as food was a mixture of sugars called "formose." For several reasons, formose has been considered in this country (4) and in Russia (12) to warrant investigation. A method for the synthesis of this material was described (13) for the first time more than a century ago. It was observed that when a dilute solution of formaldehyde was allowed to stand in the presence of lime water, the odor of formaldehyde disappeared and the solution became sweet. Subsequently (14), this sweet solution was processed carefully to yield an appreciable amount of a complex mixture of sugars, called formose. Since that time, a variety of methods have been found which can affect the conversion of formaldehyde to sugars. In aqueous solution, compounds such as $Ba(OH)_2$, PbO, $MgSO_4$, and $Ca_3(PO_4)_2$ can induce the reaction. Apparently, one role of these materials is to provide the slightly alkaline conditions required for the initial condensation of two molecules of formaldehyde to glycolic aldehyde.

$$\mathrm{HCHO} + \mathrm{HCHO} \rightarrow \begin{array}{l}\mathrm{CHO} \\ | \\ \mathrm{CH_2OH}\end{array}$$

The metal ion present also plays an important role in that, at least in the case of Ca^{++} (15) and presumably the others, it forms a complex with formaldehyde. A major competing reaction, which must be minimized for good yield of formose, is the Cannizarro reaction which results in disproportionation of formaldehyde to methanol and formic acid. The rate of this latter reaction is increased by high alkalinity, and thus limits the catalysts which may be used. The reactions subsequent to the initial formation of glycolic aldehyde probably proceed by a series of Aldol condensations and display autocatalytic characteristics. The final reaction product, glycolic aldehyde (16) or virtually any material capable of assuming an "enediol" structure (17), very much increases the reaction rate. Several schemes have been proposed to explain how these further reactions proceed to produce higher molecular weight sugars. For instance, a branched-chain reactive dimer of dihydroxyacetone has been proposed (18) as an obligatory intermediate. Other more complex schemes have been advanced (19) as possibilities. In any case, the nature of the product in aqueous phase reactions is highly dependent upon the exact conditions, catalysts, and promoters present, and an extensive literature exists concerning the predominant materials found under various conditions.

The reaction can also proceed in a heterogeneous system. Although it has been reported that Al_2O_3 is inhibitory in the presence of $Ca(OH)_2$ (15), a suspension of insoluble Al_2O_3 in dilute formaldehyde does yield appreciable amounts of sugars (20). Reactions to produce sugar-like materials in the gas phase have also been reported (21).

Finally, the nature of the energy source can be quite variable. Whereas most of the studies have been performed using heat, other types of radiation such as ultraviolet light, visible light, ionizing radiation, and coronal discharge lead to the transformation of formaldehyde either to sugars or to materials with some of the chemical characteristics of sugars.

Studies With Formose Conducted at the ARC

An apparatus was assembled which initially permitted the continuous production of about 10 g/hr of formose sugar under conditions quite similar to those described previously (15). A fresh slurry of $Ca(OH)_2$ in 4% reagent grade formaldehyde (1:10 molar ratio) was passed through a 10-meter plastic coil held at 60-65°C at such a rate as to result in the formation of a yellow color in the last few turns of the coil. After precipitation of Ca^{++} as the carbonate, filtration, deionization, and reduced pressure concentration, about a 60% yield (based upon formaldehyde) of yellow syrup with a caramel odor was obtained.

This product did not give a positive dimedone test (22) for free formaldehyde. However, after mild dilute acid hydrolysis, the presence of about 1% by weight of formaldehyde could be demonstrated. The crude formose was examined by paper chromatography and was found to contain predominately pentoses, lesser amounts of tetroses and trioses, and virtually no hexoses. Using the glucose oxidase technique, less than 0.5% free D-glucose was present in the mixture. These analytical data are somewhat surprising in light of a previous report (15) that using essentially these conditions, large amounts of hexoses including glucose were formed. The reason for this discrepancy is not immediately clear but may be related to some of the observations reported below.

It was noted that if the initial slurry of $Ca(OH)_2$ in formaldehyde was stirred at room temperature for a few days, subsequent heating to $80-85^{o}$ did not result in a reaction. The addition of reaction product did bring about a slow reaction at this elevated temperature. However, if a small amount of fresh CaO was added, the reaction rate was very much increased. Further, it was found that the reaction gave the same general distribution of product when the formaldehyde concentration was increased successively to 6% and then 8%.

By modification of the initial reaction conditions and using 8% formaldehyde, the $Ca(OH)_2 \cdot CaO$ catalyst, and a reaction temperature of $82^{o}C$, it was possible to produce formose at the rate of 50-100 g/hr. The ability to produce larger than previously possible amounts of formose permitted us to conduct the animal feeding studies described below.

It was found that the organically bound formaldehyde could be removed from the crude product. The first method involved an initial hydrolysis at 60^{o} for 30 min. as a 5% solution in 0.01 N HCl followed by addition of a large excess of NH_4OH. The hexamethylenetetramine which results from the reaction between formaldehyde and ammonia was extracted with chloroform, and the residual aqueous solution was deionized and concentrated. The second (and preferred method) involved several azeotropic reduced-pressure distillations of formaldehyde from an aqueous formose-0.01 N HCl solution followed by deionization. Extreme care had to be taken not to concentrate this mixture; otherwise, excessive discoloration and charring occurred. By both methods, the resultant product no longer gave the dimedone test for formaldehyde.

Formose Feeding Studies

Akerlof and Mitchell (15) obtained uniformly poor results when they attempted to feed their crude formose preparation to either adult or weanling rats. It is possible that the toxicity they observed was due to the presence of bound formaldehyde. In our hands, the crude preparation was also highly toxic when fed as 40% by weight of the diet. The diet itself was not optimal for the growth of weanling rats but when glucose was used as the carbohydrate source, did permit good growth (Fig. 1). It was adopted to permit total replacement of carbohydrate by the test substance and contained 51% casein, 5% corn oil, 4% salts and vitamins, and 40% glucose or test substance. Death due to the presence of crude formose occurred in 3-5 days and was accompanied by a terminal bloody diarrhea which could not be correlated with any morphological change in various sections obtained from the stomach or GI tract of moribund animals. Neither were there any major changes in appearance of sections obtained from brain, lungs, liver, spleen, lymph nodes, adrenal, kidney, testes, muscle, skin, and bone marrow. An experiment involving the addition of formaldehyde to the glucose control diet showed that a similar toxicity did not result from diets containing up to 0.5% paraformaldehyde.

Fig. 1

Thus, the presence of small amounts of bound formaldehyde in the crude formose does not explain the toxicity. Further, when formaldehyde-free formose was fed as 40% by weight of the diet, again death occurred, but in this situation, the animals survived 5-8 days. When the purified material was fed as 5, 10, 15, or 20% of the diet, very long survival and appreciable weight gain resulted but was accompanied by a persistent slight diarrhea. Thus, formose as it is presently prepared here is not suitable as food. Further efforts involving modification of reaction conditions, catalyst, etc., and chemical fractionation of the products are in progress to obtain a nutritionally adequate material. Problems related to the separation of stereoisomers and the presence of appreciable amounts of sugars which cannot be metabolized must also be investigated.

Hopefully, more selective synthetic methods can be devised which will result in the formation of a limited number of specified products, e.g., the intermediate synthesis of trioses and then their condensation to yield only hexoses.

Glyceraldehyde and Dihydroxyacetone

Another approach to supplying "carbohydrate" is to feed simple organic compounds which are normally found in the diet or present in the body during intermediary metabolism of glucose. Theoretically, these would either be oxidized and provide energy or become converted to glucose which could then be metabolized. Large amounts of trioses (as the phosphate derivative) are turned over by the body daily, and small amounts administered to animals and humans can be metabolized. Thus, Cori and Cori demonstrated (8) that dihydroxyacetone administered orally is converted by the intact animal to glucose and glycogen, although an appreciable amount also appears in the urine. About 50% of the dose was oxidized, 20% deposited as glycogen, 15% excreted, and the remainder was unaccounted for. The degree of oxidation was greater than when glucose was given, although glycogen formation was somewhat less. These data are corroborated by the studies of Tsao et al. (10). They found that in 2 hr., 28% of the radioactivity from dihydroxyacetone appeared in the expired air as opposed to 47% from radioactive glucose.

Information concerning glyceraldehyde is more limited. Preliminary evidence that it could be converted to glycogen by the liver was reported (5) by Cori and Shine. Later, Stohr (6,7) showed that feeding of 0.2-0.3 g of D, L-glyceraldehyde per 100 g body weight to fasting rats caused a rise in liver glycogen from 0.05 to 0.80% while blood sugar increased. Glyceraldehyde could no longer be detected in the blood 3 hr. after feeding. At a level of 0.2 mg. triose per 100 g body weight, the absorption of D, L-glyceraldehyde in 3 hr. was 54%, dihydroxyacetone was 68%, and pyruvic acid was 37%. The increase in liver glycogen was 63% for dihydroxyacetone, 50% for D, L-glyceraldehyde, and 34% for pyruvic acid. No problem occurred with the use of the mixed isomers of glyceraldehyde and presumably both were utilized.

The results of our efforts to incorporate significant amounts of dihydroxyacetone and glyceraldehyde into the diets of weanling rats were not promising (23). In summary, glyceraldehyde was toxic and dihydroxyacetone, while it could be tolerated as 20% of the diet, did not permit good growth. Attempts to modify the undesirable effects of this latter material by the addition of excess vitamins to the diet did not significantly change the results. Darkening of dihydroxyacetone-containing diets could be prevented by antioxidants, but to no advantage. Preparing fresh diet daily increased the toxicity. It was concluded that these trioses would not be able to meet our requirements.

Glycerol and Its Derivatives

The results of current studies with glycerol and some of its derivatives are much better than those with the materials studied previously. This is not surprising in light of work by others. In a classical study, Johnson et al. (11) refuted previous claims concerning the toxicity of glycerol and showed: (1) Normal growth of rats occurred over a period of 40 weeks when glycerol constituted 41% by weight of the diet. Normal growth also occurred with dogs fed a diet containing 35% glycerol for 50 weeks. (2) There was no detrimental effect in animals; e.g., reproduction was normal in rats, and red cell and white cell counts and hemoglobin were normal in dogs. (3) Ingestion of 110 g/day (approximately 20% of total caloric requirements) by 14 human subjects for a period of 50 days was uneventful.

Glycerol has long been known to be glucogenic and has in fact been proposed as an adjunct in the management of diabetes. More recently, radioactive glycerol has been shown to be converted almost exclusively to glucose rather than directly oxidized to CO_2 and H_2O (24,25). Studies with radioactive glycerol administered to working subjects have shown that even under conditions of high calorie utilization, most of the glycerol is still converted to glucose (25).

Our initial study with glycerol confirmed that good growth could be obtained with diets containing 40% glycerol (Fig. 1). It was also found that this concentration was the practical limit for incorporation into the diet and that 60% glycerol was toxic. Studies were then initiated with a variety of derivatives of glycerol in hopes that some of them might be better tolerated than glycerol itself. The first such studies involved triacetin which was already known (26) to be tolerated. As can be seen in Fig. 1, diets containing 40% by weight of triacetin initially permitted good growth. It should be noted that some of the differences in growth observed are probably due to variations in the consistency of the diets since glycerol and triacetin are viscous liquids. In addition, glycerol is quite sweet and triacetin is somewhat bitter.

In a different experiment (Table I), it was found that the toxicity of these individual compounds was not additive. Thus, while either 60% glycerol or 60% triacetin in the diet caused the death of most of the animals within 2 weeks, diets containing a combination of 30% glycerol and 30% triacetin or 40% glycerol and 20% triacetin permitted good growth.

Table I

These encouraging results led us to explore the possibilities of other combinations. Since effects due to osmotic pressure may have been part of the problem, diglycerol, triglycerol, and polyglycerol (Fig. 2) were fed as 40% of the diet. These materials would be expected to alter tissue osmotic pressure to a lesser degree than the monomer. Diglycerol gave essentially the same growth response as glycerol itself whereas triglycerol and polyglycerol were toxic at this level in the diet. When combinations of diglycerol and triacetin as 60% by weight of the diet were fed, the growth was poor.

Fig. 2

Better results have been obtained with monoacetin and diacetin as food for weanling rats. In the one experiment which has been conducted thus far, it appears that both of these materials are superior to triacetin as a component of the diet.

Additional studies have been conducted to determine the ability of glycerol-triacetin combinations to maintain the weight of adult animals. In some of these diets, as much as 92% of the calories were present as low molecular weight compounds. Although the first diets of this type were not capable of maintaining body weight, efforts are continuing to design such a diet.

Finally, efforts have been made to adapt the animals to some of these diets. It was felt that if the weanling animals were exposed to successively increasing concentrations of the low molecular weight compounds, their metabolism might have an opportunity to adjust and higher levels would be better tolerated. This expectation did not prove to be the case and the growth rate observed with diets containing large amounts of glycerol and triacetin was essentially the same whether the animals had been previously adapted or not.

Fats

If it were possible to synthesize acceptable fats from metabolic products, they might have certain advantages over carbohydrates or simple organic compounds. Their caloric density is about twice that of carbohydrate and therefore less would have to be made. In addition, fats are generally bland tasting and readily accepted in the diet. The major disadvantage of fats is that they cannot be incorporated into a diet as much more than 50% of the calories without producing ketosis and acidosis.

The Germans were able during 1938-45 to convert chemically a portion of the material produced by the reaction between carbon monoxide and hydrogen (Fischer-Tropsch Process) into a synthetic fat. Animal studies, while not completely convincing, did not show any major nutritional or physiological problems. This fat was subsequently consumed by the German population although the amount per capita was probably low. Again, no detrimental effects have been reported. However, the presence of odd-chain length and methyl-substituted fatty acids does raise questions concerning the levels at which these materials can safely be incorporated into the diet for prolonged periods.

We have conducted a feasibility study to determine whether technology had advanced sufficiently since 1944 to permit reliable synthesis in the space environment of fatty acids, glycerol, and fat (27). One major advance has been the development of the Zeigler Process for the polymerization of ethylene into materials which can easily be converted into fatty acids free of side chains. Improved methods are also now used commercially for the preparation of glycerol and the condensation between glycerol and fatty acids to give fats. Even though the situation with regard to the chemistry required has improved, it was the consensus of the engineers involved in the problem that the engineering constraints (control, automation, processing in zero gravity, etc.) contradict this potential food for space applications. This is not to say that the problem could not be solved but that the solution did not seem to warrant the effort and expense required, especially in light of the more favorable results obtained in feeding studies with glycerol and some of its derivatives.

World Food Problem

The studies described here are specifically directed toward the long range needs of the space program. However, the implications with regard to the predicted shortage of food in the world should not be ignored. Although the present shortage of protein in many areas of the world has attracted the greatest attention, it has been predicted that if present population trends persist, a purely calorie deficit will arise. The chemical processes required to produce the potential foods being investigated here could use as starting materials only carbon dioxide and water, both of which are in practically unlimited supply. A major requirement if these starting materials were used would be large amounts of inexpensive electrical energy such as might arise from future developments in atomic energy. This energy would be used to generate hydrogen and oxygen from the water and all the further reactions would be more or less exothermic. If any type of hydrocarbon or coal were in adequate supply, the need for electrical energy would then be minimal because the requisite intermediates could be obtained from them. For example, formaldehyde obtained as a by-product of the petroleum industry presently sells for about three cents a pound (28).

It is conceivable that chemical products of the type discussed here can be developed to the point where they will become acceptable components of the diet of the general population. This is particularly true in light of the fact that certain of these are already deliberately added to food in appreciable amounts for values other than nutritional ones and are "generally recognized as safe" (29).

ACKNOWLEDGEMENTS

The author sincerely wishes to thank Dr. David Salzberg and his associates, Arequipa Foundation, Palo Alto, California, for their well-conducted animal feeding studies; Dr. Samuel Abraham, Children's Hospital, Oakland, California, for his paper chromatographic studies with the formose preparations; and to Dr. Charles Conley, NASA, Ames Research Center, for his examination of tissue sections.

LITERATURE CITED

1. Conference on Nutrition in Space and Related Waste Problems. University of South Florida, Tampa, Florida, April 27-30, 1964. NASA SP-70 (1964).
2. Jagow, R. B., and Thomas, R. S. (eds). Study of Life Support Systems for Space Missions Exceeding One Year in Duration. Lockheed Missiles and Space Co. Contract NAS2-3012 (1966). To be published.
3. King, C. D., Johnson, W. A., and Zuraw, E. A. Study of Life Support Systems for Space Missions Exceeding One Year in Duration. General Dynamics Contract NAS2-3011 (1966). To be published.
4. Shapira, J. Design and Evaluation of Chemically Synthesized Food for Long Space Missions. Proceedings of Conference on Closed Life Support Systems. NASA, Ames Research Center, April 1966. In press.
5. Cori, C. F., and Shine, W. M. The Formation of Carbohydrate From Glycerophosphate in the Liver of the Rat. Science 82:134-135 (1935).
6. Stohr, R.: The Physiological Behavior of Trioses and Closely Related Compounds. II. Increase of Liver Glycogen After Feeding of Glyceraldehyde. Z. Physiol. Chem. 206:211-216 (1932).
7. Stohr, R.: Physiological Behavior of Trioses and Related Compounds. III. Muscle Glycogen and Blood Sugar After Feeding Methylglyoxal and Glyceraldehyde. Z. Physiol. Chem. 212:85-98 (1932).
8. Cori, C. F., and Cori, G. T. The Fate of Sugar in the Animal Body. VIII. The Influence of Insulin on the Utilization of Glucose, Fructose, and Dihydroxyacetone. J. Biol. Chem. 76:755-795 (1928).
9. Tsao, M. U., Schwartz, E. L., and Lowrey, G. H. Metabolism of Dihydroxyacetone in the Intact Rat. Metabolism 11:456-464 (1962).
10. Tsao, M. U., Bernstein, I. A., and Lowrey, G. H. Metabolism of C^{14}-dihydroxyacetone in the Intact Rat. Metabolism 11:465-469 (1962).

11. Johnson, V., Carlson, A. J., and Johnson, A. Studies of the Physiological Action of Glycerol on the Animal Organism. Am. J. Physiol. 103:517-534 (1933).

12. Sinyan, Y. Y. The Possibility of Physiochemical Synthesis of Carbohydrates in a Space. Problems in Space Biology (USSR) 3:401-409 (1964).

13. Von Butlerow, A. M. Bildungeiner Zuckerartigen Substanz Durch Synthese. Ann. 120:295-298 (1861).

14. Loew, O. Weiteres über die Condensation des Formaldehyds. J. Prakt. Chem. 34:51-55 (1886).

15. Akerlof, G. C., and Mitchell, P. W.: A Study of the Feasibility of the Regeneration of Carbohydrates in a Closed Circuit Respiratory System. Rep. no. 63143 (NASr-88), FMC Corp.; J. Spacecraft 1:303-309 (1964).

16. Kuqin, A. The Catalytic Action of Monoses on the Formaldehyde Condensation. Ber. 68:619-624 (1935).

17. Hanford, W. E., and Schreiber, R. S. (to Dupont) U.S. Pat. 2,224,910 (Dec. 17, 1940).

18. Katzschmann, E. Organic Catalysis. XXVI. Formaldehyde Condensation as an Organic Autocatalysis. 3. Reaction of Formaldehyde With Acetol. Ber. 77:579-585 (1944).

19. Pfeil, E., and Ruckert, H. Formaldehyde Condensation. Formation of Sugars From Formaldehyde by the Action of Alkalies. Ann. 641:121-131 (1961).

20. Gabel, N. W., and Ponnamperuma, C. A Model for the Primordial Origin of Monosaccharides. To be published.

21. Lind, S. C., and Bardwell, D. C. Chemical Action at Gaseous Ions Produced by α-Particles. IX. Saturated Hydrocarbons. J. Am. Chem. Soc. 48:2335-2351 (1926).

22. Vogel, A. J. Textbook of Practical Organic Chemistry, Including Qualitative Organic Analysis. Wiley, N. Y. (1962) Third ed.

23. Shapira, J., Solzberg, D. A., Young, D. R., and Conley, C. C. Pacific Slope Biochemical Conference, Eugene, Oregon, Aug. 1966. p. 9 of collected abstracts. Manuscript in preparation.

24. Nikkila, E. A., and Ojala, K. Gluconeogenesis from Glycerol in Fasting Rats. Life Sciences 3:243-249 (1964).

25. Young, D. R., Pelligra, R., Shapira, J., Adachi, R. R., and Skrettingland, K. R. Glucose Oxidation and Replacement During Prolonged Excercise in Man. To be published.

26. Cox, W. M. The Nutritive Value of Pure Fatty Acid Esters. J. Biol. Chem. 103:777-790 (1933).

27. Frankenfeld, J. W., et al. Study of Methods for Chemical Synthesis of Edible Fatty Acids and Lipids. Contract NAS2-3708. Esso Research and Eng. Corp. To be published.

28. Quotation (2-15-67) from Mr. H. Snell, Celanese Chemical Corp., Palo Alto, Calif.

29. Food Additives, Regulations. Part 121, Chapter I, Title 21 (Code of Federal Regulations). Food and Drug Administration.

Table I GROWTH OF RATS ON DIETS CONTAINING SYNTHESIZED COMPOUNDS

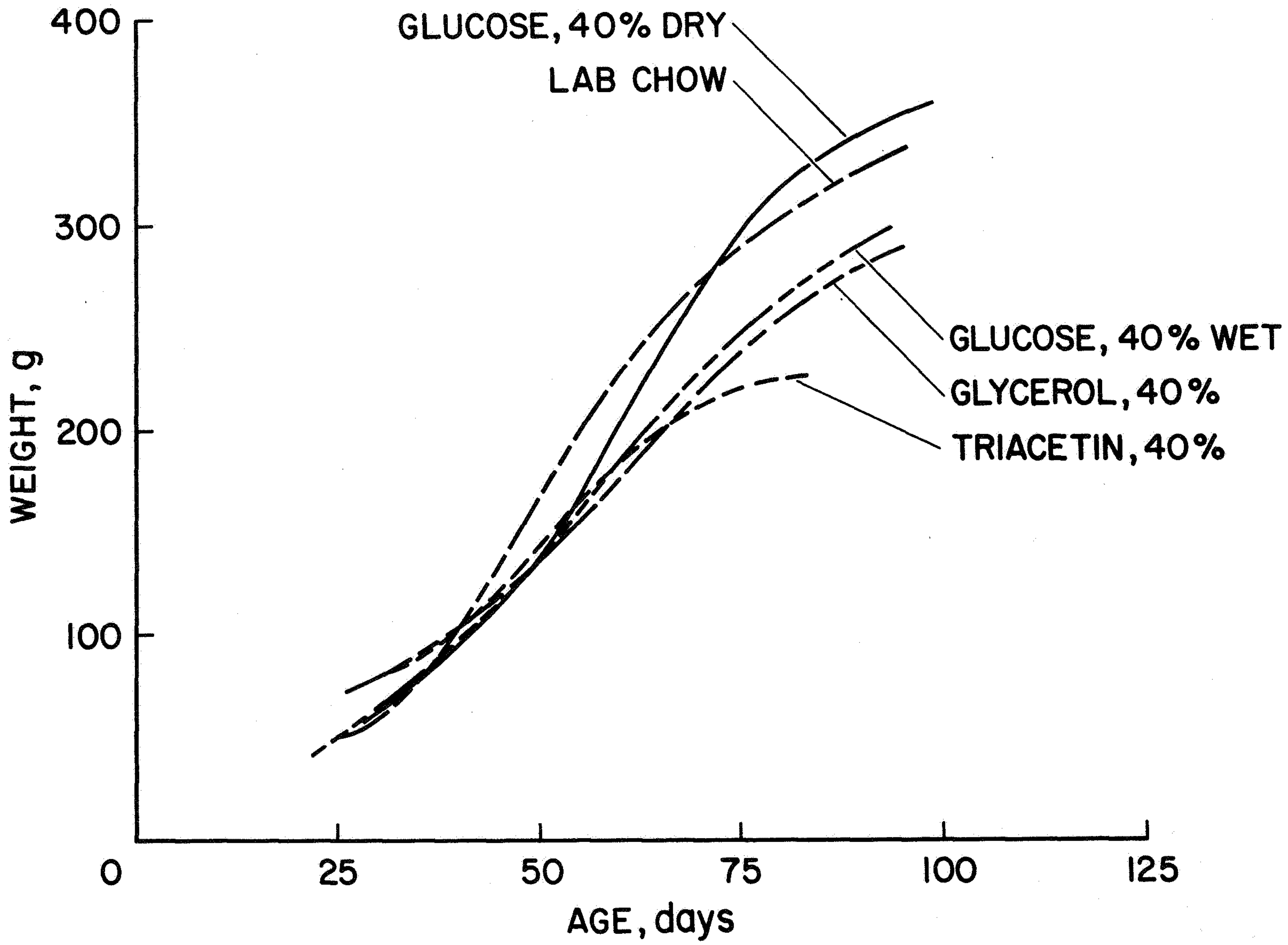
DIET		WEIGHT (G)	
		7/29	9/26
60% GLUCOSE	(6)	53 ± 2	247 ± 20
60% GLYCEROL	(6)	5/6 DEAD IN 2 WEEKS	
60% TRIACETIN	(6)	5/6 DEAD IN 2 WEEKS	
30% GLYCEROL-30% TRIACETIN	(5)	95 ± 21	245 ± 25
40% GLYCEROL-20% TRIACETIN	(6)	91 ± 20	245 ± 43
40% GLYCEROL-30% TRIACETIN	(5)	90 ± 14	172 ± 52

FIGURE LEGENDS

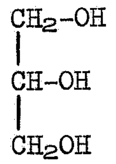
Fig. 1.- Growth of weanling rats on special diets.

Fig. 2.- Structure of glycerol and some of its derivatives.

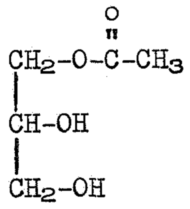
AAA082-12



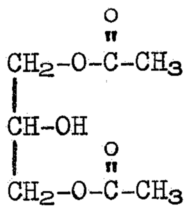
NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
AMES RESEARCH CENTER, MOFFETT FIELD, CALIFORNIA



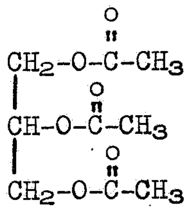
GLYCEROL



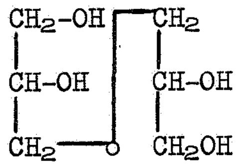
MONOACETIN



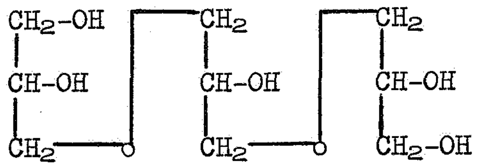
DIACETIN



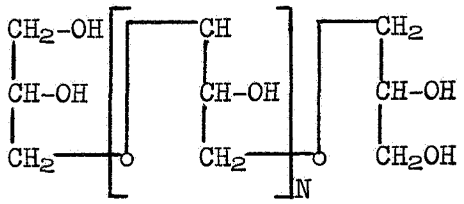
TRIACETIN



DIGLYCEROL



TRIGLYCEROL



POLYGLYCEROL