On the other hand, the object of research itself is to discover new facts and concepts for the benefit of mankind. Big business has in recent years attacked the problems of pure science with the organizational precision that American business knows so well. The result of this business method in research has been a flood of immediately practical therapies that have rudely reversed the mortality figures in many diseases. In the ethical pharmaceutical field the pattern of research, of manufacture, and of distribution have reached an efficiency that has paid off in wide human benefits.

Not the smallest part of this pattern is the widespread distribution of information on new medical products, practically a continuing postgraduate course for all physicians. Here big business has taken the very wise stand that a reputation for honesty and reliability has tangible value, and the professions have been quick to recognize the importance of this flow of service data.

From the point of view of the patient—the average citizen—I hope that your correspondent will reevaluate his estimate of the situation.

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15 July 1954.

# Interaction between Casein and β-Lactoglobulin on Heating

Electrophoretic evidence has been obtained which indicates that case and  $\beta$ -lactoglobulin, the major protein constituents of milk, combine under the influence of heat, forming a stable complex (1). When a 1 percent protein mixture composed of 0.75 percent casein and 0.25 percent  $\beta$ -lactoglobulin in 0.1 ionic strength phosphate buffer of pH 6.86 was heated at 85°C for 30 min, and electrophoresis was carried out in the same buffer, the  $\beta$ -lactoglobulin migrated with the  $\alpha$ -casein. Three well-separated electroproretic peaks (a- and  $\beta$ -case and  $\beta$ -lactoglobulin) were obtained for the unheated mixture at this pH. A solution of 0.25 percent  $\beta$ -lactoglobulin in the pH 6.86 buffer, heated in the same manner, yielded two electrophoretic peaks. The more rapidly migrating peak had a mobility slightly lower than that of the  $\alpha$ -case peak in the unheated mixture but about the same as that of the proposed complex of  $\beta$ -lactoglobulin and  $\alpha$ -case in in the heated mixture.

If  $\beta$ -lactoglobulin and  $\alpha$ -casein had not actually formed a stable complex, it should be possible to resolve the two components by performing the electrophoresis at a different pH. In an attempt to so resolve the denatured  $\beta$ -lactoglobulin and  $\alpha$ -casein components, electrophoresis of mixtures prepared and heated in the same manner was carried out in pH 2.45 glycine-HCl buffer of ionic strength 0.1. No component was present in the electrophoretic pattern of the heated mixture obtained at pH 2.45 that had the mobility of heat-denatured  $\beta$ -lactoglobulin. (Heat-denatured  $\beta$ - lactoglobulin showed a single peak at this pH.) The proposed complex, identified on the basis of the area of its electrophoretic peak, migrated with a mobility appreciably lower than that of heated or unheated  $\beta$ -lactoglobulin or unheated  $\alpha$ -casein. The area of the complex peak at pH 2.45 was not as great as the area of this peak at pH 6.86, but it was quite evident from the dissimilarities between the ascending and descending patterns that interactions of an ionic nature occurred at pH 2.45 in the heated mixture. The ionic interactions introduced considerable uncertainty into the identification of the components other than the large peak that was assumed to be the complex between  $\alpha$ -casein and  $\beta$ -lactoglobulin.

The evidence, although not conclusive, is supported by similar observations made by Jennings (2) and Krejci (3) that casein formed a complex with a horse serum immune globulin under the influence of heat.

Heat-induced interactions between proteins may be of considerable significance with respect to protein stability problems in food processing.

Work is in progress to confirm the existence of  $\alpha$ casein- $\beta$ -lactoglobulin complexes in heated synthetic mixtures and in heated and dried milk.

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#### **References and Notes**

- 1. This paper reports research undertaken in cooperation with the Quartermaster Food and Container Institute for the Armed Forces and has been assigned number 490 in the series of papers approved for publication. The views and conclusions are those of the authors; they are not to be construed as necessarily reflecting the views or endorsement of the Department of Defense.
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6 July 1954.

## Antibiotic-like Substance and Cellulose Digestion Stimulator Found in Fermented Feeds and in Rumen Fluid\*

Factors that stimulate *in vitro* cellulose digestion by rumen microorganisms have been found in fresh rumen fluid and its extracts (1-3). Cow manure and common feedstuffs have also been shown to contain similar factors (4). However, previous workers have not reported an antibiotic-like factor in these materials.

A factor, or factors, that stimulates the growth and cellulolytic activity of rumen microorganisms and inhibits the growth of microorganisms previously isolated as undesirable contaminants from the digestive tracts of ruminants has been obtained in crude form. Active extracts were prepared from four bovine ingesta, one ovine ingesta and two fermented feeds. The extracts were free of microorganisms and stable to autoclaving at a pH between 7 and 10.

Inhibition of *Micrococcus flavus* was shown by the standard plate technique for antibiotics. The extracts were further checked for bactericidal or bacteriostatic action against Pseudomonas aeruginosa and Aerobacter aerogenes by turbidity measurements.

Cellulose digestion, in vitro, was enhanced and the lag phase of washed rumen microorganisms was shortened when 0.1 ml of the extracts was added to 11 ml of the culture medium. Further studies are under way to determine the nature of the factor responsible for the inhibitory effect on contaminating microorganisms of the rumen.

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## Tarahumara Indian Piscicide: Gilia macombii Torrey

During a recent expedition among the Tarahumara Indians (1) in the Sierra Madre Occidentalis of northwestern Mexico for medical and ethnologic studies, I inquired of the Indians about the present-day use of fish poisons. Only a small number of these seminomadic, part-time cave-dwellers-those Indian families living near the Rio Conchos and other large rivers of the Sierra-still used piscicides. Among those still employed, I found Gilia macombii Torrey, a plant not previously reported to have been used as a fish poison or known to be pharmacologically active in fish or mammals.

The fish poisons previously reported from the Tarahumara Sierra by Lumholtz (2), Bennett and Zingg (3), and Clavigero (4) are summarized in Table 1.

I was told by Indian informants in the Sisoguichi and Norogachi areas of several fish poisons still in use. We were able to collect only the one called by the Tarahumara nawé and another called matéshuwa. In the area between Sisoguichi and Norogachi matéshuwa was in bloom in September 1953 in the lower land along streams. Nawé was found in the Wichaiochi area. Only the root was used as a piscicide. It is a fish poison of the genus Tephrosia (3).

Different informants in Sisoguichi, Wichaiochi, and Norogachi considered the purple-flowered plant they

Table 1. Fish poisons previously recorded.

Plant	Part used	Refer- ence
Agave sp.	Leaves	(2)
Polygonum sp.		(2)
"Palo de la flecha"	Bark	(2)
Calcalia decomposita A. Gray	Entire plant	(3)
Casimiroa edulis Llav. and Lex	Entire plant	(3)
Casimiroa sapota Oerst	Entire plant	(3)
Tephrosia talpa Wats (Synonym: Cracca talpa Wats)	Root	(3)
Sebastiania bilocularis S. Wats	Sap	(4)

called matéshuwa to be the most potent fish poison in the region. The entire plant (stems, leaves, and flowers) except the root was used by crushing the freshly gathered plant between rocks in a dammed, slowly flowing part of the stream. The Indians claim that a few armloads of the plant are sufficient to stun the fish and to cause them to rise to the surface for several hundred yards downstream. The poisoned fish may be eaten without danger.

Lyman B. Smith, curator of the Division of Phanerograms of the Smithsonian Institution, has identified pressed specimens of matéshuwa as Gilia macombii Torrey. Species of Gilia have not previously been reported as piscicides of the Tarahumara or of any other ethnic group (5), nor have toxic substances been associated with this genus in the past.

Preliminary experiments, carried out with Charles L. Wisseman of the Army Medical Center, using goldfish (sp.) weighing 3 to 5 g, indicate that a filtered, cold aqueous extract made from powdered dried plant in a concentration of 1.0 mg/ml is sufficient to stun the fish in 10 min and to kill them in less than 50 min. The fish rise frequently to the surface to swallow air, lose their equilibrium and lie on their side, and become inactive except for quick jerking movements before dying. An extract made from only 0.2 mg/ml of the dried powdered plant has killed the goldfish in 2 to 2.5 hr. Plants dried at room temperature for 3 mo were used.

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