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found that certain fatty acids and more particularly their monoglycerides were antimicrobial. Tri- and diglycerides were shown not to be lethal to microorganisms. Second, was the discovery of antimicrobial sulfonamides, first observed by Trefouel, Nitti, and Boret in Fourneau’s 1928, Fleming observed the breakdown (Iysis) of Staphylococcus bacterial colonies in an area surrounding the growth of Penicillium mold. Two important discoveries, however, occurred around this time (circa 1930). First, was the serendipitous finding by Alexander Fleming. In

products from Nature have a long and intriguing history of providing man with useful materials for his daily life. None is more important than the medium-chain fats found in mother’s milk. Mention was made in Sanskrit medicine that freshly expressed human milk was routinely used as an “antibiotic” after eye surgery. Research in our laboratory discovered that the most active lipid ingredient (monolaurin) was accountable for these antimicrobial effects. Products from Nature have a long and intriguing history of providing man with useful materials for his daily life. None is more important than the medium-chain fats found in mother’s milk. Mention was made in Sanskrit medicine that freshly expressed human milk was routinely used as an “antibiotic” after eye surgery. Research in our laboratory discovered that the most active lipid ingredient (monolaurin) was accountable for these antimicrobial effects.

Early Role of Mother’s Milk As A Nutriceutical

By definition, a nutriceutical is a functional food that has nutritional/caloric value and pharmacological (drug) effects. Hippocrates (Greek physician, circa 460-377 B.C.) recognized this truism when he declared "Let thy food be your medicine and your medicine thy food”. Historically mother’s milk must be considered the first nutriceutical. Mother’s milk not only provides the infant with important nutrients for growth and development but also it also contains substances, which have antimicrobial, antiviral and other protective properties. This concept of human milk having sanitizing effects was recognized early in human medicine. In the history of cataract surgery that extends back at least 3000 years, the translation of Hindu manuscripts gives detailed methods of the great surgeon Susruta. He described principles of surgery based on anatomic dissection. He practiced asepsis (fumigated the operating room with sweet vapors) and gave an excellent account of his technique of couching (depression of the lens into the vitreous) as well as an outline of postoperative care. After couching the milk of a nursing mother would be distributed into the eyes conjunctiva much in the way that antiseptics are used presently after an operation. Unfortunately, this knowledge was buried with the rise of Buddhism and the caste system of the Brahmains, who forbade dissection, and the shedding of blood. The surgeon gave way to the priests and the brilliant discoveries of the Hindus did not pass down to the Greeks or Egyptians. The knowledge that mother’s milk acted as an antiseptic agent was lost until recently (Fieldsteel, 1974). He found that the cream but not the skim milk was biologically active after heating. Kabara et al ( circa 1968) evaluating the structure-function properties of lipids found that certain fatty acids and more particularly their monoglycerides were antimicrobial. Tri- and diglycerides were shown not to be active. It was evident from these two studies that the non-protein portion of human milk was also biologically active since of the formation of fatty acids and monoglycerides from the lipolysis of milk fats (triglycerides). The human baby however does not posses lipases at birth while the calf is able at birth to have lipase activity on its own. Thus, human milk, in contrast to bovine milk, needs accompanying lipases from the mother to change by predigesting the inactive fat (triglycerides) into active antimicrobial fatty acids and monoglycerides.

While protein macromolecules and humoral factors are all-important antiinfecting properties of mother’s milk, emphasis here will be the discussion of the fat content of mothers milk. As will be shown in this discussion the fat content in human milk, specifically the medium-chain lipids (monolaurin), is important to its’ nutriceutical activity.

Fatty Acids and Monoglycerides as Antimicrobial Agents

Fatty acids have a long history of use as antimicrobial agents. Soaps (i.e., salts of fatty acids) have been used as cleaning and disinfecting agents for centuries. Before 1930, the lack of success in the search for active antibacterial agents other than fatty acids resulted in pessimism as to whether any other active agent would ever be found.

Two important discoveries, however, occurred around this time (circa 1930). First, was the serendipitous finding by Alexander Fleming. In 1928, Fleming observed the breakdown (lysis) of Staphylococcus bacterial colonies in an area surrounding the growth of Penicillium mold. From this observation new biochemical structures, called antibiotics, were added to the small arsenal of organic and inorganic compounds lethal to microorganisms. Second, was the discovery of antimicrobial sulfonamides, first observed by Trefouel, Nitti, and Boret in Fourneau’s laboratory (Pasteur Institute) in 1935. This gave new hope for finding new and more effective synthetic biocidal agents. These two important discoveries in less than a decade apart gave tremendous impetus to the search for new antimicrobial agents.

The biocidal activity of the newly isolated antibiotics and synthesized germicides was much greater than that of fatty acids. In proportion to the speed with which new and more powerful antibiotics and synthetic useful products were discovered, interest in fatty acids as biocides waned. The use of these more powerful "magic bullets" was accompanied by complications. First, antibiotics and synthetic germicides are not without health risks in terms of toxicity and irritation; second the cost of these newer agents precluded their use by low income people and third and most important, the improper use of these germicides caused resistant organisms to appear. Today the problem has reached critical proportions.

Today because of these shortcomings, new approaches, even those based on old technologies, need to be reexamined. This included fatty acids, which even today play an important role in food preservation. Many fatty acids more active than the old standbys such as vinegar (i.e. about 4% acetic acid (C2:0) from ancient Egypt) have been discovered. Sorbic acid (C6:2) isolated from rowanberry oil and reported in 1859 by Hoffman, the aromatic benzoic acid discovered by Fleck, and propionic (C3:0) acid have been found to be useful in food preservation. Detailed studies dealing with structure-antimicrobial effects of lipid derivatives, fatty acids and their corresponding monoesters,
have been published by Kabara in an American Oil Chemists' Society monograph (The Pharmacological Effects of Lipids, Volume I).

Much of the modern research on the germicidal activity of fatty acids was concluded between 1920 to 1940. More up-to-date studies have been reviewed (Kabara 1978, 1984 and 1997). The term "antimicrobial" is also intended to cover antibacterial, -yeast and -viral effects. It has will be shown that enveloped viruses, as Herpes and others, can be inactivated as other microorganisms by treatment with specific fatty acids. Thus, the relationships found for chain length, degree and kind of unsaturation (cis or trans) found for fatty acids against bacteria were shown to be similar to activity later found for viruses.

The antimicrobial activity for fatty acids found in mother's milk against some common microorganisms is given in Table 1. See also Welsch et al, 1979, 1981; Clarke and May (2000).

Table 1 Minimal Inhibitory Concentrations (mM) of Fatty acids found in mother's milk

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>Staphylococcus Aureus</th>
<th>Streptococcus Group A</th>
<th>Candida albicans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capric (C10, 2.0%)*</td>
<td>2.90</td>
<td>1.45</td>
<td>2.90</td>
</tr>
<tr>
<td>Lauric (C12, 10%)</td>
<td>2.49</td>
<td>0.12</td>
<td>2.49</td>
</tr>
<tr>
<td>Mvristic (C14, 6.0%)</td>
<td>4.37</td>
<td>0.55</td>
<td>4.37</td>
</tr>
<tr>
<td>Palmitic (C16, 22%)</td>
<td>NI</td>
<td>3.90</td>
<td>NI</td>
</tr>
<tr>
<td>Stearic (C18, 8.0%)</td>
<td>NI</td>
<td>NI</td>
<td>NI</td>
</tr>
<tr>
<td>Oleic (C18:1, 32%)</td>
<td>NI</td>
<td>1.77</td>
<td>NI</td>
</tr>
<tr>
<td>Linoleic (C18:2, 15%)</td>
<td>NI</td>
<td>0.09</td>
<td>0.46</td>
</tr>
<tr>
<td>Linolenic (C18:3, 0.1%)</td>
<td>1.79</td>
<td>0.35</td>
<td>NI</td>
</tr>
</tbody>
</table>

* Approximate concentration in mother's milk NI, not inhibitory at the concentrations tested (1.0 mg/ml.)

Milk fatty acids also killed L. Monocytogenes in a dose-dependent manner whereas much less killing of Salmonella (a gram-negative organisms) was observed (Sprong et al, 1999). The antimicrobial effects of individual fatty acids depended on concentration and chain length. The rank order found for human milk fatty acids was

C 14: 0 < C 18: 2 < C 10: 0 < C 18: 1 < C 12: 0

The long chain saturated fatty acids C16: 0 and C18: 0 as well as the shorter chain C4: 0, C6: 0, and C8: 0 were not active under these same concentrations.

Monoglycerides As Antimicrobial Agents

A fatty acid esterified with glycerin always increased its antimicrobial activity. Kabara extensively published details of these findings (Kabara, 1978). In all cases our conclusions of relating chemical structure to antimicrobial activity were solidly based so that later authors, many of whom never referred to our earlier papers, confirmed these structure-function relationships.

Isaacs et al (1991) added lipids previously shown to have antiviral and antibacterial activity by Kabara to human milk, bovine milk, and infant formulas to determine whether increased protection from infection could be provided to infants as part of their diet. Again fatty acids and monoglycerides with chain lengths varying from 8 to 12 carbons were found to be more strongly antiviral and antibacterial when added to milk than long chain monoglycerides. Since both cow's milk and artificial human milk are devoid of antimicrobial activity such studies suggest that increased protection from infection may be provided to infants at mucosal surfaces by the addition of antimicrobial medium chain monoglycerides to an infant's diet. Fatty acids should not be used in these instances since they are known to be irritating to mucosal tissue.

Antiviral Effects of Monoglycerides

The same structure-function relationships that were initially discovered against various bacteria, yeast, and fungi were likewise found for lipid-containing bacteriophages/viruses.

Hierholzer and Kabara (1982) reported on the antiviral aspects of monolaurin (Lauricidin®). These studies involved selected virus prototypes...
or recognized representative strains of human viruses. They elucidated virucidal effects of monolaurin on enveloped RNA and DNA viruses. Viruses that have a lipid membrane were especially vulnerable to lauric acid and its derivative monolaurin. This work was done at the Center for Disease Control of the U.S. Public Health Service.

Some of the viruses inactivated by lauric acid and its derivative monolaurin are those known to be responsible for opportunistic infections in HIV-positive individuals. For example, concurrent infection with cytomegalovirus is recognized as a serious complication for HIV positive individuals.

A number of fungi, yeast, and protozoa are inactivated or killed by monolaurin. The fungi include several species of ringworm (Isaacs et al. 1991). The yeast reported is Candida albicans (Isaacs et al. 1991). The protozoan parasite Giardia lamblia, responsible for diarrhea in babies, is killed by monoglycerides from hydrolyzed human milk (Reiner et al. 1986, Crouch et al. 1991, Isaacs et al. 1991). Chlamydia trachomatis is also inactivated by (Bergsson et al. 1998), and hydrogels containing monocaprin/monolaurin are potent in vitro inactivators of sexually transmitted viruses such as HSV-2 and HIV-1 and bacteria such as Neisseria gonorrhoea.

Most important and different from drug antibiotics is the fact that there appears to be very little development of resistance in organisms to the bactericidal effects of these natural antimicrobial lipids (Petschow et al. 1996). In fact monolaurin has been shown to reduce or prevent resistance of organisms to certain antibiotics.

The Role of Lipids on Microbial Resistance

Present data based on medium chain fatty acids (MCFA’s) and medium chain monoglycerides (MCM’s) may ideally become part of the solution to antibiotic resistance.

Using an antibiotic-resistant (R) and an antibiotic-sensitive (S) strain of P. aeruginosa, Vadehra and Wahl (1985) found that the minimum inhibitory concentration (MIC) for lauricidin® (a highly purified monolaurin) was 165 and 75 µg/ml, respectively. The MIC values for butylated hydroxyanisole (BHA) against the same organism was 210- and 115 µg/ml, respectively. Testing R and S strains of S. aureus, the MIC value were 20 and 10 µg/ml respectively, and 150 and 110 µg/ml for BHA. With both test organisms there was more leakage of the intracellular contents from S cells as compared to R cells. The involvement of the membrane as the site of action was also confirmed by the extensive leakage of hemoglobin from human and animal erythrocytes.

Flournoy (1985) found that over 100 Oxacillin-resistant Staphylococci all had the same MIC and MBC values to Lauricidin®. This indicates that antibiotic resistance can be overcome by the use of this monolaurin.

Monolaurin inhibited the induction of vancomycin resistance in Enterococcus faecalis. This non-toxic lipid was found to repress the post-exponential phase activation of virulence factor production and the induction of beta-lactamase in Staphylococcus aureus. It has been suggested that signal transduction is the most probable target for monolaurin action. Monolaurin suppresses growth of vancomycin-resistant Enterococcus faecalis on plates with vancomycin and blocks the induction of vancomycin resistance.

Conclusions

Thus, it would appear to be important to investigate the practical aspects and the potential benefit of using Lauricidin® for nutritional support for microbial infected individuals. Until now no one in the mainstream nutrition community seems to have recognized the added potential of antimicrobial lipids in the treatment of infected patients. The lipid-coated (envelope) viruses, bacteria and other microorganisms are dependent on host lipids for their lipid constituents. The variability of fatty acids in the foods of individuals as well as the variability from de novo synthesis accounts for the variability of fatty acids in their membranes. Putting special lipids like monolaurin into our diet may have adverse effects on parasitic organisms.

Most important monolaurin does not appear to have an adverse effect on desirable gut bacteria, but rather on only potentially pathogenic microorganisms. For example, Isaacs et al (1991) reported major inactivation of Hemophilus influenza, Staphylococcus epidermidis and Group B gram positive Streptococcus by monolaurin. The other potentially pathogenic bacteria inactivated by monolaurin include Listeria monocytogenes, Staphylococcus aureus, Streptococcus agalactiae, gram-positive organisms, and some gram-negative organisms (Vibrio parahaemolyticus and Helicobacter pylori). Monolaurin rapidly inactivate the latter organism which is thought to cause gastric ulcers (Petschow et al, 1996).

While there are many studies and examples for the use of monolaurin (Lauricidin®) as a topical antimicrobial agent, its systemic use for human infections is only now being vigorously investigated. Human studies underway today suggest that many antimicrobial effects found for monolaurin (Lauricidin®) in the laboratory setting are being replicated clinically when used as a dietary supplement. Individuals with genital Herpes, Hepatitis C, fungal infections, autism etc..., are being helped as witnessed by testimonials that are receive. While it is difficult to conduct double-blind experiments for dietary supplements in the real world, anecdotal positive reports from thousands of users indicate that serious consideration should be given to Lauricidin® as an important supplement for optimal health.