

Alkylglycerols

I. Traditional Art of Healing

In the folk medicine of ancient times, liver oil from certain species of shark was an important remedy among fisher folk along the west coast of Norway and also along the west coast of Sweden. It was later found that liver oil from the Greenland shark contains approximately 30% of alkylglycerols, while that from a related species, *Chimera monstrosa*, contains as much as 90%. ECOMER is refined from shark liver oil.

Within traditional medicine, it was preferably the oil from *Chimera monstrosa* which was used. The fishermen filled the emptied and cleansed stomach sacs from certain species of fish with the oil, which they kept handy to promote the healing of wounds. They also recommended the oil as a remedy for general debility and so-called irritations of the respiratory tract and the alimentary canal. It was also used for "glandular diseases", nowadays known as lymph node swellings.

In the early 19th century the use of shark liver oil almost died out, surviving only in a few fishing communities in Norway and in the Swedish province of Bohuslän. It was to take more than a century before the use of this soothing shark liver oil was revived, following the publication of scientific documentation regarding its beneficial effects.

The development of what we know today as ECOMER required the discovery of a lipid which differs from the usual fatty substances (triglycerides) by the presence of a single atom of oxygen occupying a unique position in the molecule.

II. Chemistry of Alkylglycerols

Isolation and Synthesis

The alkylglycerols were discovered by Tsujimoto and Toyama in 1922 (1). In 1926, Weidemann (2) reported that these chemical substances are characterised by a so-called ether-oxygen. The Nobel prize winner, Sir Robert Robinson, was the first to synthesise alkylglycerols, in 1930.

The synthesis of aliphatic compounds with long chains of carbon atoms represents a field of science within which the Swedish scientists Einar Stenhagen and his wife Stina Ställberg-Stenhagen have made several commendable contributions. At the institution of medical chemistry in Gothenburg, where these researchers were based, the nowadays well-known batyl-, chimyl- and selachyl-alcohol were first synthesised.

Analyses

Methods for accurate analysis are a precondition for all research and developmental work within biochemistry. This is particularly true of the alkylglycerols, traces of which are to be found in all our foods with the exception of that which is purely vegetarian. Earlier chemical analyses gave values twofold and even threefold too high for alkylglycerol concentrations. During 1940's and 1950's, more exact analytical techniques were developed, e.g. chromatography and mass-spectrometry. With these methods the Swedish researchers Hallgren and Larsson studied the presence of alkylglycerols in the human, in the cow and in elasmobranch fishes, to which the sharks belong. Their most important work, published in 1962 (6,7) and constitutes the basis for all subsequent research work on alkylglycerols performed since that time.

One very important finding of their analyses, performed with the most advanced techniques, was that the human mother's milk contains 10 times more alkylglycerols than cow's milk. The content of alkylglycerols in the daily production of mother's milk became a kind of standard optimal dosage as regards recommended intake. Another very important finding was that shark liver oil also contains methoxy-substituted alkylglycerols possessing important biological qualities.

III. Biological and medical effects of alkylglycerols

Alkylglycerols and the Function of Bone Marrow

Holmes (3) was the first to discover that bone marrow contains one of the alkylglycerols: batyl alcohol. Later, Olof Sandler showed that synthetic batyl alcohol has the same effect on red blood cell production as a bone marrow fraction with a high concentration of batyl alcohol. Although Sandler's work was of a pioneering nature, it is astonishing that his discoveries were so little talked about at the time.

Astrid Brohult showed early on that leukopenia and thrombocytopenia, which are an inevitable consequence of radiation therapy, can be prevented - or at least reduced - by taking alkylglycerols during the course of irradiation. Johan Brohult has recently performed studies on the effect of alkylglycerols upon the production of granulocytes and thrombocytes in the bone marrow.

Alkylglycerols and Treatment of Carcinoma of the Uterine Cervix

In a vast research project at Radiumhemmet in Stockholm, Astrid Brohult was able to show that patients with carcinoma of the uterine cervix, who had received alkylglycerols before the primary radiation treatment as well as throughout the course of external irradiation, had a significantly better survival rate than patients who were not given alkylglycerols.

As a result of a collaboration between Astrid Brohult and Ingemar Joelsson it was also found that radiation injuries, which usually develop during the course of irradiation, can be reduced with as much as 60% as a result of taking alkylglycerols.

Alkylglycerols in Conjunction with Radiation Therapy

Much of the research work carried out on alkylglycerols during the last couple of decades has concerned their use in the cure of carcinoma of the uterine cervix. We therefore sense a real need to elucidate this topic. It is necessary to distinguish between the effects which follow the administration of alkylglycerols only during the course of conventional radiotherapy for carcinoma, and those effects which can be achieved if the administration of alkylglycerols starts prior to the treatment and continues throughout the period of therapy.

Leukopenia and thrombocytopenia invariably occur during the course of irradiation. These changes in the relative proportions of blood cells can be neutralised or counteracted by the ingestion of alkylglycerols, even if taken only during the course of treatment. Moreover the "pure" radiation-induced injuries occur in a statistically significantly lower frequency, the reduction amounting to a maximum of 60%.

Very important - and to a certain extent unforeseen - results were achieved, however, when alkylglycerols were taken for a period before radiation therapy commenced. Even if taken for so short a period as 5-7 days, the more advanced stages (stage IIB - IV) of the tumour regressed toward less advanced stages. This is in fact a kind of effect upon tumour growth and its spread. The same effect of alkylglycerols has been demonstrated in experimental studies on mice in a laboratory environment.

In her doctoral thesis "Aloxyglycerols and their use in radiation treatment", Astrid Brohult showed early on that alkylglycerols were of value in connection with the treatment of carcinoma of the uterine cervix. The most significant findings reported in her thesis are the following:

- The reduction in number of white blood corpuscles (leukopenia) seen in connection with the radiation treatment became less pronounced within the group of patients for whom alkylglycerols were prescribed.
- When the irradiation caused a bone marrow malfunction (regarding the production of nucleated corpuscles) the intake of alkylglycerols changed the picture radically. Yet a more liberal intake of alkylglycerols did not lead to any overproduction of thrombocytes.
- The patients with carcinoma of the uterine cervix who were treated with alkylglycerols both before and during the radiation treatment had a 10% better survival rate (as determined 5 years after the commencement of therapy) than the patients in the control groups.

The results of these investigations were so encouraging that it was felt necessary to continue with further studies on the effects of alkylglycerols on the survival rate of patients with carcinoma of the uterine cervix. In these further studies, alkylglycerols were given in such a high dose as 600 mg per day. In the first studies, reported above, the dose was 300 mg/day. In these extended studies the beneficial effect on survival rate and on the decrease in development of radiation induced damage were confirmed.

Alkylglycerols and Immunology

Bo Hallgren and his co-workers, Gunnel Stållberg and Bernt Boeryd discovered the methoxy-substituted alkylglycerols in shark liver oil and out-lined and proved their very important biological effects. Hallgren was able to synthesise several of these methoxy-substituted compounds. Together with Boeryd he has reported in a series of scientific papers, that the methoxy-substituted alkylglycerols have an inhibitory effect on the growth of tumour cells in vitro and are capable of limiting or even arresting the growth and spread of experimental tumours in mice.

As alkylglycerols are abundant in the organism of animals, chiefly in bone marrow, liver, spleen and in human mother's milk we wished to investigate the effect of alkylglycerols, and especially the methoxy-substituted compounds, on the body's immunological defence system.

Among the results we would just mention that immunoreactivity was stimulated by a very small addition to the diet, of pure methoxy-substituted alkylglycerols derived from shark liver oil or synthetically produced. When the complete range of alkylglycerols from shark liver oil was used, the proportion had to be increased towards 3% of the diet.

The stimulating effect of methoxy-substituted alkylglycerols on the blood-bound (humoral) immunoreactivity, dependent upon the production of antibodies, has recently been elucidated in several experimental studies conducted by Hallgren and Boeryd. It is of great interest that the immunoreactivity can also be stimulated in the off-spring through their mother's milk. This was shown in cases when methoxy-substituted alkylglycerols were administered to the mothers during the lactation period.

The effect of methoxy-substituted alkylglycerols on the cell-bound immunity amongst animals has been investigated by applying various techniques, all generally accepted and acknowledged as reliable. Even the tissue-bound immunity was stimulated to a very high degree by adding methoxy-substituted alkylglycerols to the diet.

As can be seen, alkylglycerols, taken together with the usual food intake, stimulate the immunoreactivity of the body. In laboratory experiments it was also shown that methoxy-substituted alkylglycerols had a definite effect upon various species of bacteria, this effect being similar to that of antibiotics. The antibiotic effect and its degree is similar to the one seen in connection with the use of nitrofurantoin. The substances also have an inhibitory and even killing effect upon fungi, especially the fungi which attack the skin.

Connection between the Effects of Alkylglycerols on Tumours and on the Immunological System

In clinical praxis as well as in animal experiments with various transplanted or chemically induced tumours, alkylglycerols have been shown to inhibit the growth and spread of the tumours. Even in *in vitro* experiments with cell cultures, the alkylglycerols have a very well documented tumoricidal effect.

It is really very interesting that one and the same substance, shown to be effective in connection with ingestion of food, possesses both immuno-reactivity stimulating and tumour-inhibiting potency. In addition to the methoxy-substituted alkylglycerols, this has been shown for very similar chemical substances which have been studied at the Max-Planck Institute for Immunology in Freiburg. These substances have also been used at the Department of Hematology and Oncology in Munich.

Tumour cells are known to have a very low content of ether-splitting enzymes. Consequently alkylglycerols can be incorporated into the cell membrane together with phospholipids. The tumour cells, however, are surrounded by cells in the body's own defence system, the macrophages. These cells penetrate the vessel walls and attack the tumour cells in tissues. They can destroy the cell membrane and can kill the tumour cell, possibly just by virtue of their very high content of ether-splitting enzymes.

Radioactive waves and radiomimetic substances attack tumour cells quite differently. Both attack the nucleus of the cell. When alkylglycerols, according to the hypothesis outlined above, attack the membrane, the two mechanisms can work synergistically and this might be the real background for the very pronounced effect upon the healing in tumour diseases and upon the increase in survival rate achieved in connection with treatment of carcinoma of the uterine cervix. Under no circumstances it is suggested, however, that carcinoma of the uterine cervix differs in this respect from any other malignant tumour in the body.

Ever since 1950 there has been an accumulating body of information regarding the effects of alkylglycerols upon common diseases such as influenza and infections.

Even such diseases as asthma and psoriasis have been cured in patients after they begun to supplement their food with alkylglycerols.

Even though one can not draw any specific conclusions from these observations, the reported healing has in several instances been quite remarkable.

Several scientific projects are now under way in Sweden and elsewhere to penetrate deeper into the mechanisms of the biological and medical effects of alkylglycerols.

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