Biological effect of ether-lipids

Alkylglycerols

by

Professor Ingemar Joelsson, MD, PhD

The Institution of Obstetrics and Gynecology
University of Umeå
Umeå, Sweden
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Ether lipids are chemical substances with a pronounced biological activity. The alkylglycerols are closely related to glycerol, the main difference being that one of the hydro- gen atoms (H) in one of the three OH-groups in glycerol molecule has been replaced by a rather long chain, most often represented by the letter R in the chemical formula.

\[
\begin{align*}
\text{CH}_2\cdot \text{OH} & \quad \text{CH}_2\cdot \text{OH} \\
\text{CH} \cdot \text{OH} & \quad \text{CH} \cdot \text{OH} \\
\text{CH}_2\cdot \text{OH} & \quad \text{CH}_2 \cdot \text{O} \cdot \text{R}
\end{align*}
\]

This so called R-chain consists of carbon-hydrogen groups with 16 to 18 carbon atoms. It is called an ‘aliphatic’ chain — the word aliphatic is of Greek origin and means ‘like in fat’ or ‘derived from fat’.

Depending on the configuration of the R-chain, there are several ether-lipids within the family of alkylglycerols. Three of the most common alkylglycerols are named Chimyl-alcohol, Batyl-alcohol and Selachyl-alcohol. The number of carbon atoms in the aliphatic chain varies between 16 and 18 and the number of hydrogen atoms between 33 and 35.

- Chimyl alcohol: \( R = (\text{CH}_2)_{15} \cdot \text{CH}_3 \)
- Batyl alcohol: \( R = (\text{CH}_2)_{17} \cdot \text{CH}_3 \)
- Selachyl alcohol: \( R = (\text{CH}_2)_{8} \cdot \text{CH} = \text{CH} \cdot (\text{CH}_2)_{7} \cdot \text{CH}_3 \)

It is very characteristic that these three alkyl-glycerols have a methyl group at the end of the chain. Selachyl-alcohol is, however, different from the other two, in that there is a so called ‘double bond’ in the middle of the chain, this alcohol is ‘unsaturated’.

Certain alkylglycerols are special: they possess a methoxy-group (\( -\text{OCH}_3 \)) in the beginning of the aliphatic chain. The methoxy group replaces a hydrogen atom.

Even though the alkylglycerols in general have very profound biological and metabolic activity, the methoxy-substituted alkylglycerols are known to be much more potent that the others.
Based upon laboratory tests and animal studies as well as upon research work done in conjunction with the administration of alkylglycerols to human beings, certain effects exerted by the alkylglycerols have been ascertained or guaranteed. These effects are the following:

The intake of alkylglycerols:

1. Prevents the decrease in number of white blood cells, leading to leukopenia, which regularly occurs during radiotherapy. The leucopenia is a result of damaged bone marrow function as a result of irradiation.

2. Prevents the decrease in number of platelets (thrombocytes) during irradiation or the administration of cytostatic agents. This thrombocytopenia is also a result of an adverse effect upon the bone marrow function.

3. Results in a marked increase in survival rate – measured 5 years after the initiation of therapy - in patients with carcinoma of the uterine cervix.

4. Significantly reduces the frequency of injuries due to radiation for malignant diseases.

5. Enhances the immunological response in general and promotes the formation of antibodies.

This effect number 5 — the stimulation of the immunological system is especially connected to the presence of the methoxy group in the methoxy-substituted alkylglycerols. These have been shown in several studies to stimulate the immunological system and modulate/enhance the immunological response to various agents.

**Methoxy-substituted alkylglycerols:**

- Immunostimulation
- Immunomodulation

The methoxy-substituted alkylglycerols also have antifungal as well as antibiotic activity.

**Methoxy-substituted alkylglycerols:**

- Antibiotic activity
- Antifungal activity

The antibiotic activity has been characterized as similar to the effect of the well-known pharmaceutical agent nitrofurandatin.

In cell cultures in the laboratory, it has been clearly demonstrated that the methoxy-substituted alkylglycerols have a direct cytotoxic effect upon tumor cells. In animal studies – using rats and guinea-pigs as test objects – this effect has been verified. Malignant tumors in the rat were shown to progress at a slower rate if the animal was fed alkylglycerols. Also, metastases, i.e. spread of the tumor to distant sites, were seen more infrequently.

**Methoxy-substituted alkylglycerols:**

- Cytotoxic effect on tumor cells
- Inhibiting effect on tumor growth
- Inhibiting effect on tumor spread
One of the largest studies regarding the effect of alkylglycerols in the human was conducted at the Radiumhemmet in Stockholm. Ecomer, a product containing alkylglycerols as well as methoxy-substituted alkylglycerols, was used in the study. Several thousands of patients with various stages of carcinoma of the uterine cervix took part of the investigation.

When analyzing the results, it became evident that one had to differentiate between the effect of alkylglycerols given during the conventional radiotherapy and the effect of the glycerols, when the administration had begun already before the initiation of radiotherapy and was allowed to continue during the course of the therapy.

The most dramatic effect of alkylglycerols was bound to the regimen of starting the intake of the glycerols before radiotherapy and continuing during and after the therapy. In the group of women, taking alkylglycerols in such a fashion, the five year survival rate was shown to be 65% while in the group of women who did not take alkylglycerols, the 5-year survival rate was only 50%, which is a statistically significant difference.

![Bar chart showing the effect of alkylglycerols compared to the control group at start and 5 years.]

If the intake of alkylglycerols did not begin before radiotherapy, there was virtually no effect upon survival.

But – on the other hand – even if the intake did not start before radiotherapy – a strong and significant effect upon the adverse reactions of radiotherapy was shown. Most strikingly, the leukopenia and thrombocytopenia, which almost always accompany radiotherapy, was inhibited. The bone marrow function became normalised by the intake of alkylglycerols.

This effect upon the bone marrow function can be seen very clearly in the next figure, depicting the decrease in number of white blood cells during the years 1952 and 1953 in a nurse at the Radiumhemmet in Stockholm. She was constantly subject to small doses of radiotherapy and her white blood cell count was decreased. Upon the intake of Alkylglycerols during late 1953 and four times during the first half of 1954, her bone marrow function was normalized.

This is very important, alkylglycerols normalizes the function – it never overstimulates the bone marrow function.
Ecomer should be taken as a supplement to food. Usually 50 mg of alkylglycerols are present in the standardised shark liver oil within a capsule of gelatin. In prophylactic use, the intake of one to two such capsules 2 to 3 times a day is recommended. But during the cure of a disease, the amount of alkylglycerols taken daily can be doubled. In the studies from the Radiumhemmet in Stockholm, the dose of alkylglycerols amounted to 600 mg per day.

**Formulation:**

250 mg standardized shark liver oil
(equivalent to 50 mg alkylglycerols)
in soft gelatine capsules

**Dosage:**

1 – 2 capsules 2 – 3 times daily
This is 0.5 – 1.5 g oil or
100 – 300 mg alkylglycerols

The intake of alkylglycerols has never been shown to cause any negative side effects. As a matter of fact, alkylglycerols are constantly being produced within the own body. In a diseased condition, however, such as infections, allergic diseases or tumors, the need of alkylglycerols is evidently greater than can be provided for by the own production. Under these circumstances, the intake of additional amounts of alkylglycerols are important in order to prevent the disease and to achieve a faster and more reliable cure.
Alkylglycerols are present in the human bone marrow, in the liver, in the spleen and in the 'mother's milk'. In comparison with the content of alkylglycerols in those sources, the content in shark liver oil is dramatically higher. Therefore, shark liver oil has been chosen as the raw material for alkylglycerols when it comes to the production of for example Ecomer. But it is necessary to remember that the alkylglycerols are obtained from the oil after the use of sophisticated procedures. The oil is refined, standardised and a technique called molecular distillation is applied.

Alkylglycerols in nature:

Human bone marrow  0.2 % of the lipids
Human milk          0.1 % of the lipids
Cow's milk           0.01 % of the lipids
Shark liver oil      10 - 30 % of the lipids

Ecomer is not just another shark liver oil preparation. Ecomer is the name of purified ether lipids – alkylglycerols – with exceptionally strong biological effects.