

Introduction of  **CETO3**TM
Cetoleic acid & Omega-3

CETO3®はノルウェーGrøntvedt Biotech社がニシンオイルをベースに開発した新規性オイルです。

極長鎖脂肪酸であるオメガ11脂肪酸/セトレイン酸 (C22:1n-11) を18%以上含有するユニークな機能性オイルとして2023年に上市しました。 (*DHA/EPAをそれぞれ6%ずつ含有)

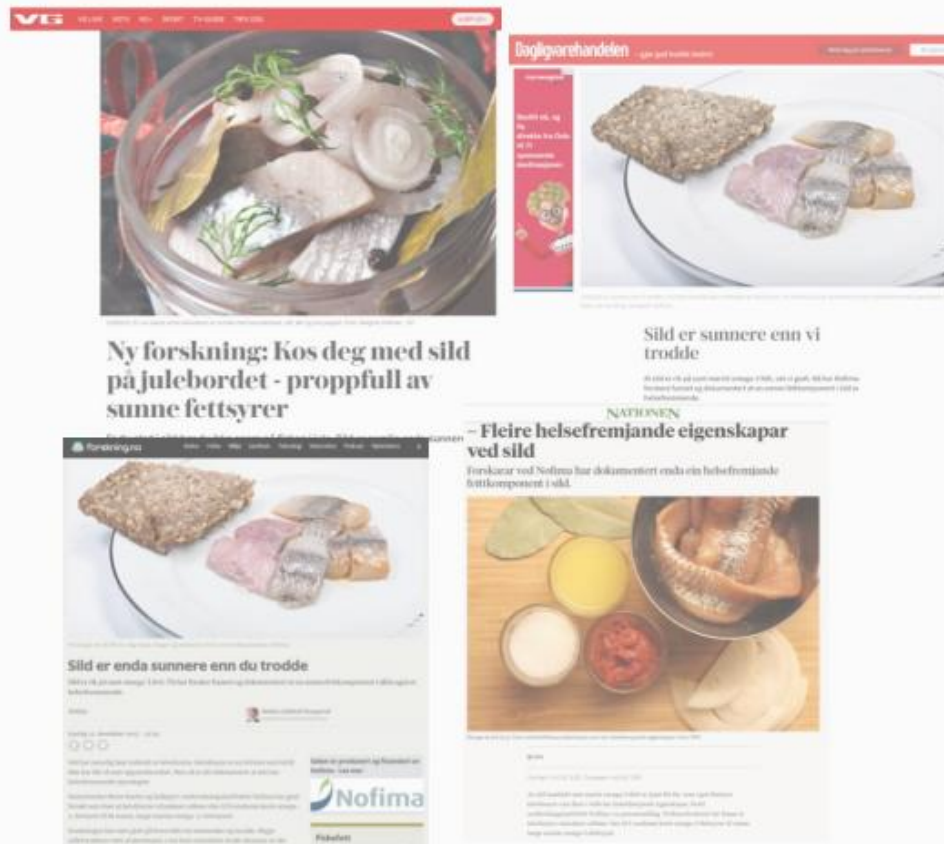
Norwegian Seafood research fundとの協業の下、オメガ11脂肪酸の特異性を活かして、スキンケア効果、抗炎症効果、心血管予防効果 (アテローム性動脈硬化症/コレステロール) および脳関連疾患の軽減効果、などを対象にヒト臨床試験を合計7つ計画・実施中です。



ニシン由来のオメガ11/セトレイン酸は、欧州メディアでも“新規性の健康オイル”として注目を集めています。

Norwegian media

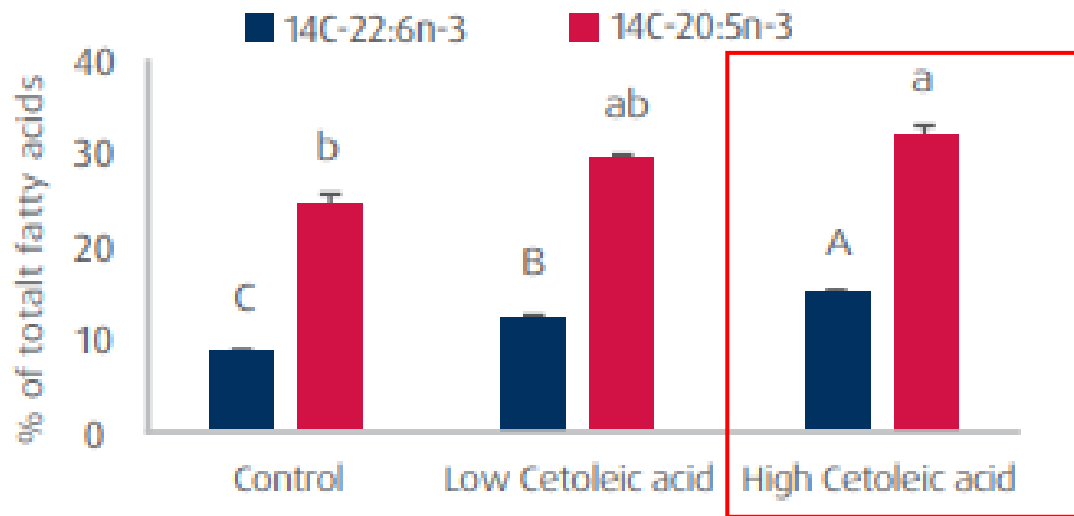
International media



又、セトレイン酸は、ヒト肝細胞におけるDHA及びEPAの合成を加速します。

ヒト肝臓細胞株 (HepG2) にセトレイン酸を濃縮した実験では、 α リノレン酸からのDHA/EPA産生を約**40%増加**させました。

Human liver cells (HepG2) EPA and DHA



Cetoleic acid in North Atlantic fish oils stimulate the synthesis of EPA and DHA from ALA in human liver cells and salmon

North Atlantic fish oils from herring, sand eel and capelin are characterized by high levels of the long chain monounsaturated fatty acid cetoleic acid (22:1n-11) and moderate levels of the healthy fatty acids EPA and DHA. New results show that cetoleic acid has bioactive properties being able to stimulate the conversion of the α -linolenic acid (ALA) to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in several species.

Background

With the estimated future growth in the world aquaculture production and the increase in human population, there will probably be a lack of Ω -3 fatty acids for production of both fish feed and Ω -3 products for human consumption in near future. It is therefore of high importance to develop strategies to enhance the utilization of existing EPA and DHA sources by improving the different species' innate capacities for EPA and DHA production from the shorter chain Ω -3 fatty acid ALA.



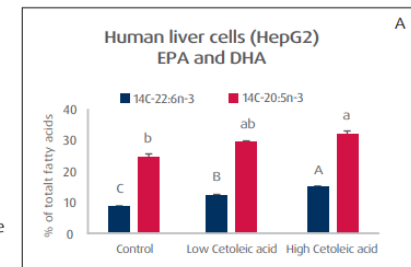
Herring from the North Atlantic. PHOTO: TOMMY ELLINGSEN GNOFIMA

Trial designs of *in vitro* and *in vivo* studies

The effect of cetoleic acid on the Ω -3 fatty acid pathway was investigated in two different *in vitro* cell models; a human liver cell line (HepG2) and primary salmon liver cells. Further, the cetoleic acid was tested as part of a North Atlantic herring oil in two separate salmon feeding trials. In the first feeding trial the salmon was fed two levels of either herring oil or sardine oil containing high or low levels, respectively, of cetoleic acid. The EPA and DHA levels in the diets were balanced. In the second feeding trial the salmon were fed three different inclusion levels of either herring oil or sardine. In these diets the total sum of EPA+DHA was balanced, but the ratio between EPA and DHA in the herring and sardine diets were different. The herring diet was higher in DHA, whereas the sardine diet was higher in EPA. This was done to investigate if cetoleic acid could compensate for the known inhibitory effect of DHA on the Ω -3 fatty acid synthesis.

Results: Cetoleic acid stimulates the EPA and DHA synthesis in human and salmon liver cells.

Enrichment of a human liver cell line (HepG2) and salmon primary liver cells in culture with cetoleic acid, resulted in approximately 40% and 11% increased production of EPA and DHA from ALA, respectively (Figure 1).



英国にて実施された12週間に及ぶヒト臨床試験では、

- CETO3摂取グループ（1,000mg x2/日、n=14）は
- 通常の魚油摂取グループ（1,000mg x2/日、n=16）

と比較して、体内のオメガ3インデックス*を魚油摂取グループと比較して、**50%高める***ことが分かりました。

* 赤血球膜中のEPAとDHAの合計を総赤血球脂肪酸に占める割合で表した指標。生物学的変動性が少なく、直近のオメガ3系脂肪酸摂取量に影響されないという特徴がある。心血管疾患予防の観点からは、オメガ3指数が4%未満は高リスク、4~8%は中程度リスクであり、8%以上の場合に低リスクとされている。

* CETO3摂取群のカプセルにはDHA/EPAが400mg/日配合、魚油摂取グループには同600mg/日が配合（+50%）。体内のDHA/EPA増加量は同様であった。

The screenshot shows a website page for 'nbnutraceutical' with a 'Vitafoods India' event banner. The main article is titled 'Grontvedt looks to boost Omega-3 index by 50%' and is dated 3-Oct-2023. The article text states: 'Grontvedt Biotech has unveiled a new branded ingredient backed by an Omega-3 index study, conducted on a CETO3 group and a fish oil group'. Below the text is a large image of two golden capsules. To the right of the article is a sidebar with 'Featured Companies' (Faravelli, Kemin, Mibelle Biochemistry, PLT Health Solutions, Beneo, Lallemand Health Solutions, Sabinsa, Gencor, PhytoGaia Sdn Bhd, Nutriventia) and 'Related Content' (Grontvedt Biotech launches ingredient brand CETO3, Grontvedt Biotech to exhibit for the first time at SupplySide West).

2018年にチェコ共和国で実施したヒト臨床試験では、被験者100人を対象に6カ月間CETO3（1g/日）を摂取させました。

試験開始時の平均オメガ3インデックスは5.1%でしたが、試験終了時点では同10.7%と**2倍増加**しました。

平均DHA/EPAも +112%となりました。

又、研究対象者の83%において、オメガ3インデックスを低リスクもしくは中リスクに改善させ、心血管リスクを低減する可能性があることを示しました。

Cardiology

Clinical research

Herring oil intake results in increased levels of omega-3 fatty acids in erythrocytes in an urban population in the Czech Republic

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Abstract

Introduction: The prevalence of cardiovascular diseases is relatively high in Central European countries, which may be caused by unhealthy dietary habits and cigarette smoking. The traditional Czech diet is low in seafood – a food reported to offer some reduction of risk for myocardial infarct and stroke. The European Health Authority recommends regular intake of fish or food supplements providing at least 250 mg of the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) daily.

Material and methods: The present study included 100 subjects from Prague not eating fish. They were given herring fish oil capsules providing approximately the recommended dose of EPA + DHA for 6 months. Omega-3 and other fatty acids were analysed from red blood cells (RBC) before and after study completion. Study parameters were omega-3 index, EPA + DHA, and the atherogenic index comprising saturated fatty acids divided by unsaturated fatty acids.

Results: Mean omega-3 index at study entry was 5.1% ($p < 0.01$) increasing to 10.7%, while mean EPA + DHA increased by 112% ($p < 0.01$).

Conclusions: Capsules of herring oil containing 250 mg EPA + DHA daily increased RBC content of omega-3 fatty acids, increasing the omega-3 index to low or intermediate risk values in 83% of the subjects studied. In populations with low access to or no tradition of eating fish, herring oil capsules providing the EU recommended dose of omega-3 fatty acids might reduce cardiovascular risk as indicated by the surrogate parameter omega-3 index.

Key words: fish oil, Atlantic herring, eicosapentaenoic acid, docosahexaenoic acid, omega-3 index, inflammatory index, atherogenic index.

Introduction

Cardiovascular morbidity is relatively high in Central European countries. Risk factors such as cigarette smoking, hypertension, diabetes, and total cholesterol elevation are common among both sexes in the Czech Republic [1]. Intake of seafood, fruit and vegetables is low compared to many other European Union member countries. The traditional Czech diet is mainly based on pork meat, potatoes, flour dumplings and bread.


① α リノレン酸→EPA/DHAを亢進

- ・ α リノレン酸→EPA/DHAの律速段階である α リノレン酸→ステアリドン酸の過程に関わる $\Delta 6$ デサチュラーゼの活性を高める、と予想しています。
- ・ ヒト肝がん細胞株HepG2を用いた、放射性同位体の炭素で標識した α リノレン酸がセトレイン酸存在下で EPA/DHAになる率が高い、とのデータから蓋然性が高いと判断しています。

② EPAはペルオキシソーム増殖剤活性化レセプター (PPAR α) のリガンド

- ・ PPARはパーオキシソーム/ペルオキシソームを増やす事に関連する因子であり、PPAR α リガンドはコレステロール低下にも作用し得ます。
- ・ パーオキシソーム/ペルオキシソームが増える事で、極長鎖脂肪酸を含めた脂肪酸の処理が進み、また、DHAの合成が進むと考えられます。
- ・ PPAR α は血管内皮でも発現し、SOD（活性酸素を消去する酵素）の発現に関与する事で、過酸化物の蓄積にも関与すると考えられます。

一般魚油との比較

	 CETO3™ <small>Cetoleic acid & Omega-3</small>	魚油 (EPA 18% : DHA 12%)
ALAからDHA/EPAへの亢進作用	◎	
白色脂肪組織 (体内の余剰脂肪) の低減作用	○	
肝臓脂肪を低減作用	○	
脂肪組織と肝臓に対する抗炎症作用	○	○
PPARと結合しての脂質代謝及び炎症調整	○	○
GLP-1増加(食欲とインスリン感受性に関係) * ノボ ノルディスクのダイエット薬と同作用機序	○	
LDLコレステロールの低減作用	◎	
中性脂質 / 血中トリグリセリドを低減作用	○	○
内皮機能の改善 (血流改善)	○	○
動脈硬化予防作用(マーカー : TMAO値の低減)	○	

LDLコレステロール低減効果に関するヒト試験を2024年8月開始予定。N=80、8週間。
動物試験では▲15%低減効果を実証。



Pre Clinical Lowering LDL Cholesterol study turn into clinical study with start August 2024 funded by Norwegian seafood research fund (FHF)



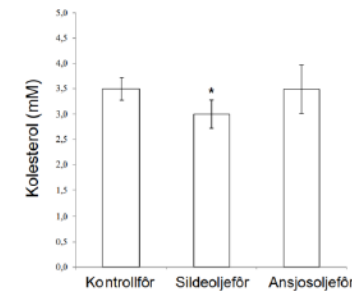
Diabetiske rotter - førinnhold

Anchoveta Oil no detection of Cetoleic acid/Omega-11

Pre clinical study shows signifiant reduction of LDL Cholesterol of 15%.

	Kontrollfôr	Sildeoljefôr	Ansjosoljefôr
Ketolinsyre (g/100g fôr)	ND	0,88	ND
EPA+DHA (g/100g fôr)	ND	0,44	0,44
Kolesterol (mg/100 g fôr)	17,5	21,2	20,1

Kolesterol i blod fra diabetiske rotter



- Clinical study study of Pelagic fish effect on Cholesterol.
- 80 persons/cps /8 weeks
- **Start August 2024**

Klinisk studie

- Undersøke effekten av sildeolje på kolesterolnivået i folk
- 80 personer med overvekt/fedme
- Kapsler med sildeolje/kontrollolje i 8 uker
- Blodprøver før og etter
- Starter august 2024

スキンケア効果に関するヒト試験を実施済。n=24にて、プラセボ比較で乾燥肌・湿疹症状が有意に改善。論文は現状未公表。

Science

Unpublished

skin study; A Randomised, Two-armed, Double-blinded Nutritional Study of Cetoleic acid/Omega-11 on Skin Quality in Healthy Women



Sample photo.
Skin measurements were taken from the face using a VISIA skin analysis instrument.

A skin study pilot trial with 24 women randomised to using a product with 10% Cetoleic acid/Omega-11 or corn oil placebo in a double-blind placebo controlled, randomised study to assess effects on healthy skin. In this study, the redness of skin was statistically significantly reduced in those taking 10% Cetoleic acid compared to placebo. This indicates that an anti-inflammatory activity of Cetoleic acid is also relevant in skin.

Dosage 4 x 1 gram capsule
Cetoleic acid: 10%

In conditions where the skin lacks the ability to make MUFA, the skin is characterised with poorly developed sebaceous glands which normally keep the skin from drying. This provides an indication of the importance's of MUFA in the skin biology.

<https://ichgcp.net/clinical-trials-registry/NCT05128240>

ノルウェー水産開発ファンドを活用して、前述のLDLコレステロール低減（動脈硬化）効果についてヒト試験を実施予定、スキンケアについては同じく前述の未公表ヒト試験のほか、乾癬症状への効果を細胞試験で実施中。脳機能に関するヒト試験についても計画中。アルツハイマー（3型糖尿病）に関する動物試験結果についても2024年中に論文公表予定。

Norwegian Seafood research fund health benefits focus for Omega-11



Cardiovascular

Significant reduction of LDL Cholesterol/mainting HDL levels

Good results on pre clinical Atherosclerosis

Increase of omega-3 index 5.3% to 10,7%



Brain Health

Positive Alzheimer/Diabetes 3 pre clinical study to be published during 2024.



Skin Health

CETOSKIN Enzema study ongoing

Psoriasis Cell study

Project number	Study	Duration	Status
901846	Effect of Cetoleic acid from north atlantic pelagic fish on psoriasis (KETO4CELLS)	2023-2025	Ongoing
901592	Health effects on Cetoleic acid (22:1n-11) Dietary intervention) in a mice and humans.	2020-2024	Ongoing
901710	Targeting atherosclerosis by cetoleic acid (22:1n-11): Dietary intervention studies in patients and mice	2022 - 2026	Ongoing
901769	Assessing the effects of cetoleic acid from pelagic fish on insulin sensitivity, fatty liver and diabetic neuropathy	2022 - 2025	Ongoing
901786	Clinical effect on dry skin and eczema using oil rich in cetoleic acid (CetoSkin)	2022 - 2024	Ongoing
901353	North atlantic pelagic fish effect on utilization of Omega- 3 EPA/DHA	2017 - 2020	Complete

欧州



欧州



米国



豪州



Thank you so much for listening to us



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