

Omega-rich oils are efficient against malaria, but may enhance viral infections.

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In a 1Q2020 review paper we described the strong antimalarial properties of polyunsaturated fatty acids (PUFA), but also raised some concerns about the potential risks for viral infections.

Jérôme Munyangi, Pierre Lutgen, Artemisia plants, arachidonic and other polyunsaturated fatty acids. Malaria World Journal, MWJ 2020, 11:3

Fish oils are rich in polyunsaturated fatty acids, often of the so-called omega-type. Some of them like docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), arachidonic acid (AA) cause marked *in vitro* growth inhibition of *Plasmodium falciparum*. Parasite killing is significantly increased when oxidised forms of polyunsaturated fatty acids are used. Saturated fatty acids are less effective because they are more resistant to oxidative attack. It is even likely that oxidation of polyunsaturated fatty acids is a defense mechanism of the host. Similar effects were seen *in vivo* on mice infected with *Plasmodium berghei* and treated during 4 days with these acids. The effect is not only prophylactic but also suppressive.

During malaria infection the parasite tries to eject PUFA from the erythrocyte.

Fatty acid	Duck erythrocytes	<i>Plasmodium iophura inf</i>	Monkey erythrocytes	<i>Plasmodium knowlesi inf</i>	Rat erythrocytes	<i>Plasmodium berghei inf.</i>
16 : 0	24	26	22	34	24	42
18 : 1	18	33	18	36	8	21
20 : 4	10	3	17	2	31	5
22 : 6	7	3	2	<1	-	-

Fatty acids (%) of the total lipids of normal erythrocytes and of infected erythrocytes

L M Kumaratilake, A Ferrante, B S Robinson, T Jaeger, and A Poulos. Enhancement of neutrophil-mediated killing of Plasmodium falciparum asexual blood forms by fatty acids: importance of fatty acid structure. Infect Immun. 1997 Oct; 65(10): 4152–4157

M Krugliak, E Deharo. Antimalarial effects of C18 fatty acids on Plasmodium falciparum in culture and on Plasmodium vinckei petteri and Plasmodium yoelii nigeriensis in vivo. Exp Parasitol. 1995 Aug;81(1):97-105. doi: 10.1006/expr.1995.1097.

V Zuzarte Luis, J Mello-Vieira. Dietary alterations modulate susceptibility to Plasmodium infection. Nature Microbiology, 2017, 2, 1600–1607

But what is positive in the case of malaria, may be negative in the case of viral infections.

Some COVID-19 patients go on to develop severe infection with organ failure, potentially leading to death, and one of the contributing factors appears to be toxicity from the release of stored unsaturated fatty acids (PUFA), according to a small study in Gastroenterology.

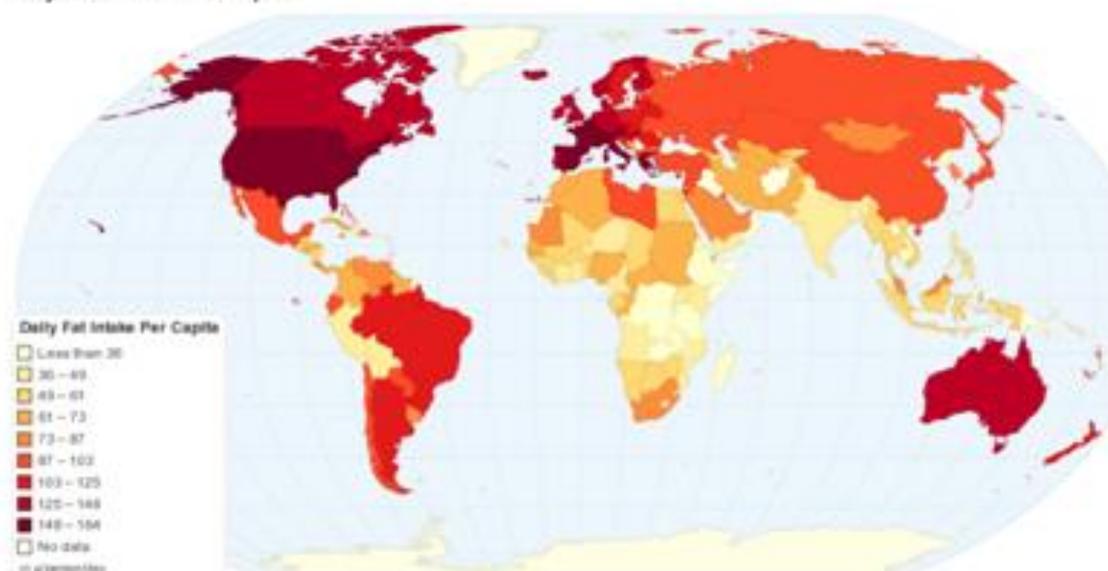
Separately, on analyzing global COVID-19 mortality data and comparing it with 12 risk factors for mortality, they found unsaturated fat intake to be associated with increased mortality. This was based on the dietary fat patterns of 61 countries in the United Nations' Food and Agricultural Organization database. Surprisingly, they found saturated fats to be protective.

Humans have 1 to 5 kilograms of linoleic acid stored in fat. In this stored form it's safe, but it is released by lipases in pancreatitis and in COVID-19 infections. The lethal dose of free linoleic acid is 280 milligrams per kilogram. This dose may be reached by the addition of linoleic acid from external sources

El-Kurdi B, C, Cartin-Ceba R, Singh VP, Onbehalf of the Lipotoxicity In COVID-19 Study Group, Kostenko S, Trivedi S, Folmes C, DykhouseKM, Babar S, Chang Y-H, Pannala R, Cartin-Ceba R, Mortality from Covid-19 increases with unsaturated fat... Gastroenterology 2020, , doi: <https://doi.org/10.1053/j.gastro.2020.05.057>.

PUFA also affect obesity, and not all obesity is the same. It is the PUFA component in obesity that determines the degree of harm in the event of acute lipolysis as in severe COVID-19 or acute pancreatitis. And this strongly depends on the staple food in a given region. Fat intake is much lower in Africa and this may explain the higher malaria endemicity in this continent.

Daily Fat Intake Per Capita



Lutgen P. *New insights into malaria prophylaxis. Pharm Pharmacol Int J.* 2017;5(6):213-217. DOI: 10.15406/ppij.2017.05.00141

Review of the evidence available in published literature supports a radical change in viewpoint with respect to disease in countries where maize is the predominant dietary component. In these countries, the pattern of disease is largely determined by a change in immune profile caused by metabolites of dietary linoleic acid.

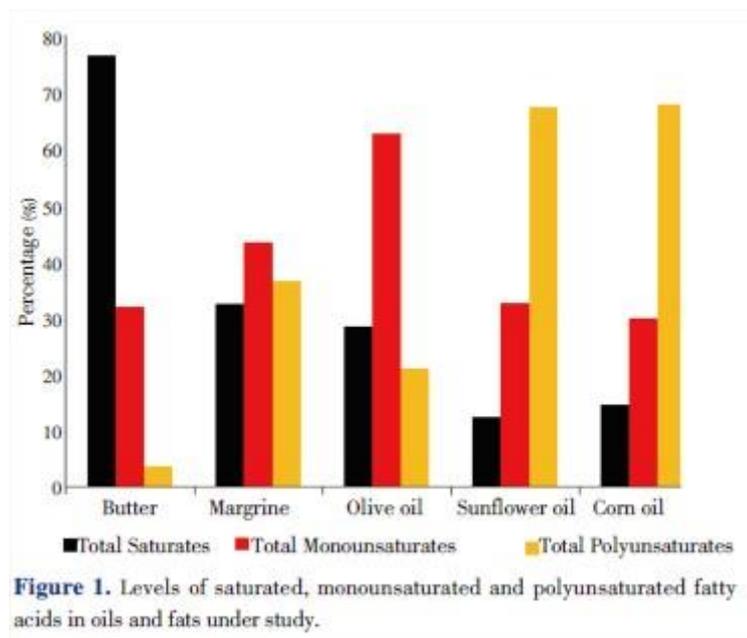
Sammon A. *Dietary linoleic acid, immune inhibition and disease. Postgrad Med J.* 1999 Mar; 75(881): 129–132.

If the administration of linoleic acid raises some concerns in viral infections, it is prudent not to recommend the use of Artemisia herbal remedies, a plant very rich in linoleic acid. See my recent weblogs published on www.malariaworld.org

Pierre Lutgen. *Viruses, Malaria, Platelets and Artemisia. May 23, 2020*

Pierre Lutgen. *Malaria inhibits Covid. June 10, 2020*

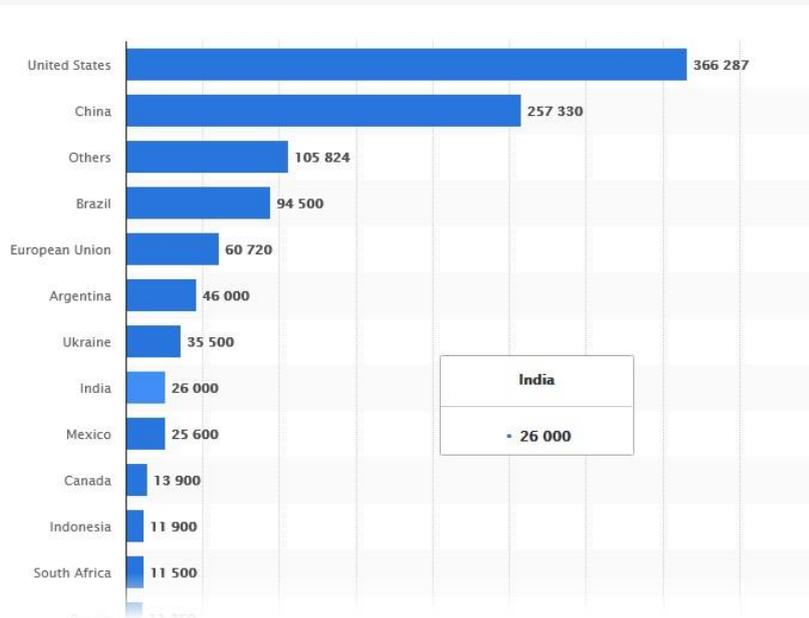
Corn is one of the plants richest in PUFA and this table food may have a positive impact on malaria and a detrimental effect on viral infections



Mohammad El-Sayed Yassin El-Sayed Haggag , *Impact of dietary oils and fats on lipid peroxidation in liver and blood. /Asian Pac J Trop Biomed* 2014; 4(1): 52-58

Global corn production in 2018/2019, by country

(in 1,000 metric tons)



The detrimental role of linoleic acid has been confirmed in another recent paper : A direct structural link between SARS-CoV-2 spike and linoleic acid, a key molecule in inflammation, immune modulation and membrane fluidity. The presence of linoleic acid was confirmed in several binding pockets of the SARS-CoV-2. Regarding the potential impact of remodeling on fluidity and elasticity of biological membranes, the composition of phospholipid bilayers is a key element in maintaining surface tension in lungs, and alteration of lipid composition is observed in acute respiratory distress syndrome and severe pneumonia, both of which are key symptoms of SARS-CoV-2 infections. The high affinity, high specificity linoleic acid scavenger function confer a tissue-independent mechanism by which pathogenic coronavirus infection drives immune dysregulation and inflammation.

Christine Toelzer, Kapil Gupta, Sathish K.N. Yadav, Unexpected free fatty acid binding pocket in the cryo-EM structure of SARS-CoV-2 spike protein, Preprint BioRxiv, June 2020.

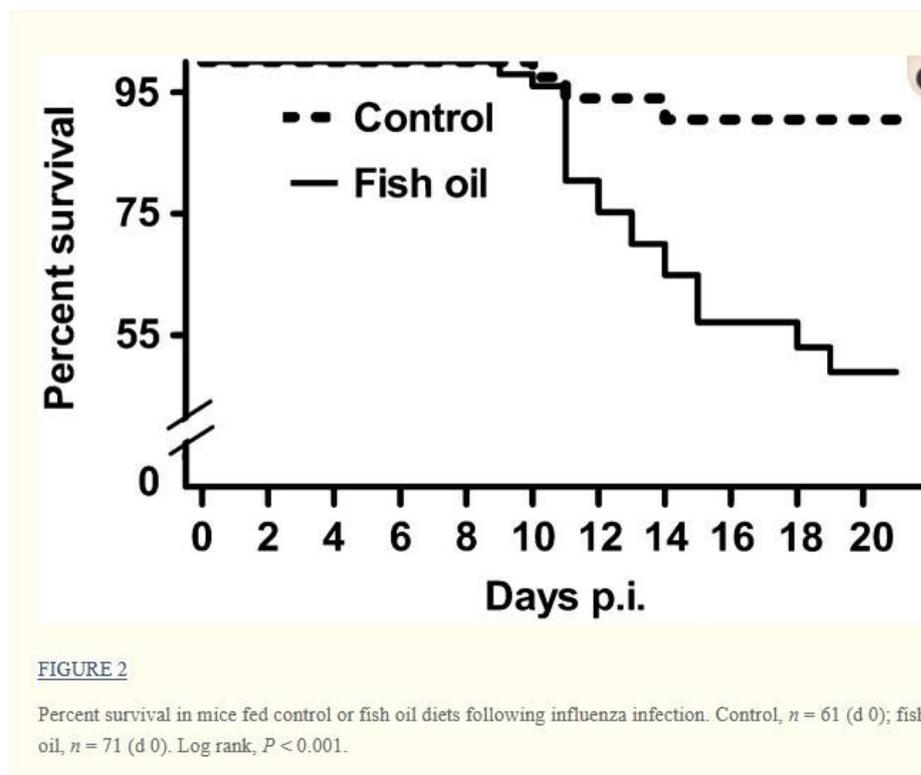
Paul M. Byleveld, Gerald T. Pang, Fish Oil Feeding Delays Influenza Virus Clearance and Impairs Production of Interferon- γ and Virus-Specific Immunoglobulin A in the Lungs of Mice The Journal of Nutrition, Volume 129, Issue 2, February 1999, Pages 328–335.

If unsaturated fatty acids increase the viral load, saturated fatty acids are inhibitors. Just the opposite as for malaria.

David Y.-W. Lee, Xudong Lin, Palmitic Acid Is a Novel CD4 Fusion Inhibitor That Blocks HIV Entry and Infection. AIDS Res Hum Retroviruses. 2009 Dec; 25(12): 1231–1241.

Zhang R, Pan Q, Zhang Z, Cao H, Saturated Fatty Acid Inhibits Viral Replication in Chronic Hepatitis B Virus Infection Hepat Mon. 2015 ; 15(5):e58828.

Already in 2009 a study showed that fish oil feeding increases virus load in the lung, because the fish oil-fed mice had reduced inflammation in the lungs and the inflammatory response is necessary for viral control. On day 7 p.i., fish oil-fed mice had a viral load that was 7.1-fold higher than that of controls.



Nicole M. J. Schwerbrock, E. Karlsson. *Fish Oil-Fed Mice Have Impaired Resistance to Influenza Infection.* *J Nutr.* 2009 Aug; 139(8): 1588–1594.

PUFA are highly prone to oxidative degradation. The role played by these degradation products urgently needs further investigations.

David Cameron-Smith, Benjamin B. Albert *Fishing for answers: is oxidation of fish oil supplements a problem?* *J Nutr Sci.* 2015; 4: e36.

Omega-3 businesses have been warned about the dangers of making immunity claims during this Coronavirus crisis. The US Food and Drug Administration (FDA) and Federal Trade Commission (FTC) are closely watching for misleading product claims around COVID-19 prevention or treatment and even a general “immunity” claim on a product could be considered an implied claim about COVID-19.