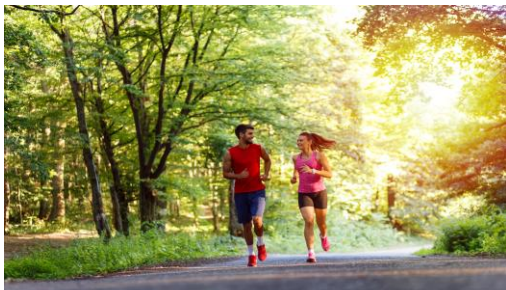


5-HM FACT SHEET: FOOD, FEED & PHARMA

5-Hydroxymethylfurfural, a promising substance for the development of innovative products in the fields of food and feed additives and pharmaceuticals.



Functional Food and Dietetic Additives are fast growing markets with lower barriers to entry compared to pharmaceuticals and therefore much faster go to market possibilities.



Novel Pharmaceuticals represent a growing and interesting future market for 5-HMF as a promising active pharmaceutical ingredient (API).



The success of the food and drinking ingredients industry can best be seen by the triumph of the energy drink segment. 5-HMF is a promising ingredient for the next generation energy drink.

5-Hydroxymethylfurfural (5-HMF, CAS NO. 67-47-0) is mainly generated by acid-catalysed thermal dehydration of fructose and identified as a flavouring substance in a wide variety of heat-processed products. 5-HMF is accredited within [EU regulation for flavouring substances](#) used or intended for use in or on foodstuff. It also occurs in wood smoke and smoke flavourings ([Morales 2009](#)). Levels of 5-HMF can be very high in certain foods such as dried fruits or caramelised products, exceeding 1 g/kg ([Journal of Agricultural and Food Chemistry 58 \(12\): 7317–22](#)) and can also be found in heat-sterilised glucose/fructose solutions for parenteral nutrition. Based on these facts, 5-HMF has been used for some time in food analysis as a marker substance for quality assessment, e.g. in the analysis of honey or wine, where high 5-HMF levels occur when these products undergo a long period of storage or overheating during the production process ([J. Agric. Food Chem., 2014, Volume 62, Issue 5, pages 1159–1166](#)).

5-HMF can also be found in significant quantities in [heat-processed Chinese Herbal Medicines \(CHMs\)](#) such as Lycium chinense, Cornus officinalis, Rehmanniae radix, Polygonum multiflorum, and Schisandra chinensis. CHM had been prescribed clinically for thousands of years. Currently, CHM is gaining increased attention around the world, due to its distinguished therapeutic effects with minimal or negligible side effects.

In the last decades, there has been intense debate concerning 5-HMF's toxicity, mutagenicity, and carcinogenicity. Therefore, the content of 5-HMF in honey, beer, and coffee has been strictly limited. In the meantime, a number of studies have shown that these concerns are not valid anymore. In a [statement from the German Federal Institute for Risk Assessment](#) (Bundesinstitut für Risikobewertung, BfR), the substance was determined to be safe and to pose no risk to humans, based on the existing experimental studies of the acute toxicity or carcinogenic and mutagenic effect of 5-HMF. K. Abraham et al published a review on the Toxicology and risk assessment of 5-Hydroxymethylfurfural in food ([Mol. Nutr. Food Res. 2011, 55, 667–678](#)).

Upon oral ingestion, 5-HMF shows no toxic metabolites in humans, according to a study, which underscores its safety for use ([Journal of Separation Science 2013, 36, 670-676](#)).

Adverse to the previous concerns on the potential danger of 5-HMF, the theory on a positive biological activity of 5-HMF in humans and animals emerged in recent years.

Not only that 5-HMF is not toxic, it appears to be quite the opposite: based on what we know today, 5-HMF is a substance with extremely positive effects on the human body ([British Journal of Haematology, February 2005](#)). The ability of the substance due to its structure to bind with haemoglobin and exert a positive influence on the binding capability of oxygen has already found use as a possible treatment for sickle cell anaemia.

In 2014 Baxter (now Baxalta) took over AesRX, a company who developed the drug Aes-103 for the prophylactical treatment of sickle cell anemia. The active component is 5-HMF. [Clinical studies](#) up to phase IIb were executed, where test persons were administered with up to 8 grams of 5-HMF per day. The maximal daily uptake through conventional food products (e.g. honey, fruit juices etc.) is estimated at 350 mg.

5-HMF also consumes singlet oxygen in an oxidation reaction and binds other dangerous reactive oxygen species (ROS) like hydroxyl or superoxide-radicals. Medically speaking, this substance has a wide

range of uses. For example, the symptoms of patients with lung cancer given perioperative 5-HMF in addition to a nutrition programme improved significantly ([Eur J Cardio-thoracic Surgery 2007; 32: 776](#)).

This ability of 5-HMF to improve the supply of oxygen to tissues and counteract oxidative stress, has been proven in a range of studies. For example, in the animal model, the substance significantly extended the length of survival of mice with permanent cerebral ischaemia ([Neural Regen Res. 2012 Aug 5;7\(22\):1722-8](#)). The symptoms of insufficient supply of oxygen from external influences e.g. exposition at high altitudes or various diseases, can also be drastically improved with the administration of 5-HMF ([WO2013012670A1](#)).

Oxidative stress, caused by intermediately formed reactive oxygen species, is responsible for an entire range of diseases. Thanks to the capabilities of HMF-5 described above, 5-HMF is currently being intensively investigated for its use in the treatment and/or prevention of various medical problems. These include, for example, the treatment and prevention of alcohol-related liver damage ([Int. J. Mol. Sci. 2015, 16, 2446-2457](#)) or the use of the substance for neurodegenerative diseases ([Neural Regen Res 2013;8:2605-14](#)).

Free radicals are also formed disproportionately in diabetes by the process of glucose oxidation. The finding of another study highlights the pharmacological application of 5-HMF for preventing cardiovascular and diabetes mellitus diseases and provides the theoretical basis for further development of a therapy for diabetes-associated vascular diseases ([Food Chem. 2013 Sep 1; 140 \(1-2\): 273-279](#)).

In a further study the properties of 5-HMF were confirmed to be natural antioxidants and were examined for their effects on cancer cells. Here the substance showed a clear antiproliferative effect on certain cancer cell lines ([J Agric Food Chem. 2013 Nov 6;61\(44\):10604-11](#)), which brings to the fore its possible use as a preventative measure against certain types of cancer.

The fact that the administration of 5-HMF often elicits an immune response has led some researchers to suggest its use as an immunostimulant, e.g. in the treatment of HIV (Cambridge, MA [mit-7.88j](#), [Protein Folding and Human Disease, held by Dr Jonathan King on 9 April 2015](#)).

Current research reveal the cardioprotective effect of 5-HMF in I/R that is mediated by inhibition of L-type Ca²⁺ channels ([Br J Pharmacol. 2017 Oct;174\(20\):3640-3653](#)).

5-HMF as a carbonyl compound can also bind free amines and ammonia and remove them directly in the metabolism process. Ammonia is generated during long and intensive physical exertion and affects both the musculature and mental concentration. The use of 5-HMF can therefore improve physical and mental performance.

The results of all these studies show that 5-HMF can be used as an ideal nutritional supplement or as the basis for new, innovative pharmaceuticals to improve mental and physical performance in healthy humans as well as in animals. Amateur athletes as well as professional sportsmen can achieve improved training efficiency when 5-HMF is used as a supplement as shown by Gatterer et al. ([J of Dietary Supplements 2018 Oct 22](#))

