Fermented wheat germ extract

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Abstract and key points

- Fermented wheat germ extract (FWGE) is produced from wheat germs of the genus Triticum vulgaris.
- The active ingredient in FWGE is not yet known.
- It has been claimed that orally used FWGE offers beneficial effects for cancer patients during chemo- and/or radiotherapy.
- The evidence from clinical trials to support claims of efficacy is weak.
- The oral intake of FWGE seems to cause no harm.

Fermented wheat germ extract (FWGE) is industrially produced and in clinical use. The production of FWGE involves fermenting wheat germs of the genus *Triticum vulgaris* by adding baker's yeast (*Saccharomyces cerevisiae*). The medically active substances of FWGE are not yet known.

It has been proposed that 2,6-dimethoxy-p-benzoquinone and 2-methoxy benzoquinone found in wheat germ might act antiproliferative because of its high redox potential. FWGE is believed to increase efficacy of chemo- and radiotherapy, to reduce its side effects and to improve quality of life.

Although eight controlled clinical trials consistently reported positive results, the evidence for the claimed benefits is very weak, due to high risk of bias in trials published to this date. No placebo-controlled trials have been carried out.There is no toxicity known by the intake of FWGE. Side effects are rare and mild.

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What is it?

Description

Wheat germ is the embryo portion of the wheat kernel. It is a concentrated source of vitamins, minerals, and protein, and is sustained by the larger, starch storage region of the kernel—the endosperm. During the production of wheat flour, the wheat germ is usually removed. In whole wheat products, however, the wheat germ is either not removed or added again after processing. Fermented wheat germ extract (FWGE) is industrially produced and in clinical use.

Scientific names/brand names

FWGE involves fermenting wheat germs of the genus *Triticum vulgaris* by adding baker's yeast (*Saccharomyces cerevisiae*). FWGE is produced as an over-the-counter drug in more than ten countries and sold under the names Avemar, Avemar pulvis, Ave Ultra, MSC and Ave.

Ingredients

The production of FWGE involves fermenting (i.e. transforming sugar into ethanol by microorganisms) wheat germs of the genus Triticum vulgaris by adding baker's yeast (Saccharomyces cerevisiae), adding filtered air and controlling the pH-level and temperature. The process takes about 18 hours. The dried product which is available on the market contains 63.2% FWGE and as technological additives 35% maltodextrin and 1.8% kolloidal silicondioxid[1,2,3]. Dimethoxy-p-benzoquinone is used to standardize and robustify the production process and amounts up to 0.4 mg/g are found in the final product. 2-Methoxy benzoquinone can also be detected in the final product[4].

Application and dosage

FWGE is dissolved in water and applied orally. The author's of clinical trials used dosages of FWGE ranging from 8.5 g once to 9 g twice daily[5,6]. In a study of children the authors administred 12 g/m2/day[6]. A dose of 8.5 g/day contains 1.7 mg of 2,6-dimethoxy-p-benzoquinone which is equivalent to the consumption of 700 g of whole wheat bread[4]. According to the U.S. Department of Agriculture, individuals who are on a diet primarily based on whole wheat products have a daily intake of about 15 g wheat germ[7,8].

History and providers

The idea of using FWGE for medical purposes was introduced by Hungarian Nobel laureate for medicine Dr. Albert Szent-Györgyi. He proposed the conjecture, that the benzoquinone found in wheat germ might act antiproliferative because of its high redox potential[9,4]. Later, a way of industrially producing FWGE was invented and patented by Hungarian biochemist Máte Hidvegi.

Mechanism of action/alleged indications/claims of efficacy

No single substance has been found that could explain the claimed antimetastatic, apoptotic and immune modulatory effect of FWGE. While Szent-Györgyi attributed the main effect to benzoquinones, it seems now most unlikely that these are the main active ingredients[4,10].

n vitro studies and animal studies (partly unpublished) suggest different mechanisms of action. Explanations of the effectiveness of FWGE include, i) impeding the repair mechanisms of chemotherapy-induced damage in the DNA (inactivation of poly (ADP-ribose) polymerase)[4], ii) improving the tumor defence of the body (impeding major histocompatibility complex class 1 expression)[4], increasing intercellular adhesion molecule 1 expression[11] or iii) impeding the growth of malignant cells by changing the metabolism (change in pentose phosphate pathway)[12,13]. Apoptosis induced by FWGE[14,15] and additive/synergistic effects of FWGE with 5-FU, Oxaliplatin and Irinotecan on different human cell cultures were observed in several in vitro studies[16]. FWGE is used as a supplement to chemo- and radiotherapy in the treatment of solid, malignant tumors, as it is believed to improve both the success of treatment, as well as patients' quality of life[5,6,17]. Furthermore, there are claims that FWGE can be used in chemotherapy to reduce the risk of neutropenic fever[18].

Prevalence of use

The exact prevalence of use of FWGE is not known.

Legal issues

FWGE is available as a nutrient supplement in many countries.

Cost and expenditure

Daily dosage costs up to **€ 4** at current prices.

Does it work?

Eight controlled clinical trials in adults were carried out with patients diagnosed with head and neck cancer, malignant melanoma, and colorectal carcinoma and in children with diverse malignancies[5,6,17,18,19,20]; they are described in **Table 1**. All trials reported benefits of FWGE treatment: two studies found longer overall and progression-free survival times[5,6], two studies identified reduced relapse rates[18], three trials showed improved quality of life[5,17,18] and another study found reduced incidence of febrile neutropenia[18]. However, the evidence that treatment with FWGE confers benefits to cancer patients is very weak, as all study data were at high risk of bias: only one study was a randomized clinical trial and all studies were open labelled, had small sample sizes, and poor reporting quality. All trials used the same patented FWGE from one manufacturer.

Is it safe?

Studies in animals showed neither toxicity nor mutagenic potential of FWGE[3].

Adverse events

The American Food and Drug Administration (FDA) considers FWGE to be safe[21]. Side effects of FWGE include diarrhoea, nausea and vomiting, flatulence and constipation[5].

Contraindications

There are no known contraindications.

Interactions

In vitro experiments and animal studies showed no pharmacological interactions with agents used for chemotherapy[22].

Warnings

There are no known warnings.

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Dietary approaches