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Research Article

Revisiting the Budwig Diet Protocol with Recent Research Findings Authenticate it as an Effective Evidence Based Anticancer Therapy

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Abstract

Budwig Diet, developed in the early 1950s by the German chemist Dr. Johanna Budwig (1908–2003) was a popular alternative cancer therapy during her periods when there was no any effective conventional therapy existing for treating Cancer. Although it is still widely practiced all over the world for cancer treatment as an evidence based alternative therapy, it is not an approved drug by the FDA for treating cancer. However, the evidence-based therapies are popular in Asian and African countries and people are using them as the main or alternative therapy for various diseases especially for cancer. In order to validate its use as an evidence-based therapy for cancer treatment, the anti-cancer properties of the active ingredients present in the Budwig Diet are analysed for their anti-cancer properties with recent scientific findings and clinical trials.

Keywords

Budwig Diet, Evidence based anticancer therapy, Omega 3 fatty acids, Thiols.

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Introduction

Budwig Diet, developed in the early 1950s by the German chemist Dr. Johanna Budwig (1908–2003) was a popular alternative cancer therapy during her periods when there was no any effective conventional therapy existing for treating Cancer. Even today, due to ineffective treatments and fear of severe side effects in the present conventional cancer therapies, people seek some alternative therapies. The use of complementary and alternative medicines including dietary supplements, herbals and special diets to prevent or treat disease continues to be popular. In that way, the Budwig Diet protocol is still a popular alternative therapy and people practice it worldwide (https://budwigcenter.com/). However, it is neither scientifically validated nor approved by FDA. While science was not advanced enough to substantiate Budwig's claim during her time, she, as a popular biochemist was able to interpret some scientific principles behind her findings. Although recent scientific findings have invalidated some of her interpretations on the working mechanisms of her diet's ingredients against Cancer, many scientific findings are being continuously added in recent years supporting the anticancer properties of the ingredients such as flax seed oil, cottage cheese that contained in her Diet formula. Those recent scientific findings help to evaluate the anti-cancer therapeutic value of her treatment protocol. Mannion C, et al. [1], while preparing their therapeutic formula for treating cancer by bringing some improvements in Budwig Diet formula, have attempted to highlight some scientific facts behind the Budwig Diet protocol. Following this, Paulraj S [2] has brought further evidences supporting Budwig's findings with some more recent scientific reports. In the last decade, a large number of new clinical trials were conducted to validate the effectiveness of ω3 PUFAs in cancer therapy [3]. As many more such scientific findings have been added till date due to the advancement of science, it is proposed to revisit the Budwig Diet protocol with latest research findings which will add further strength for considering it as an effective evidence-based cancer therapy.

Ingredients of Budwig diet and their anticancer properties as envisaged by her

Based on the works of the Nobel Prize Laureate Otto Warburg (1931), the several times Noble Prize nominee Budwig opined that the main factor for the development of cancer was a low oxygen environment in the tissue which she believed to be caused due to the deficiency of sulphydryl groups and/or a fatty acid partner, that enhance cellular respiration. They are present in cottage cheese and flax seed oil respectively [4]. According to her, by regularly consuming them, one can enrich oxygen supply there by inhibit the formation of cancer cells.

Budwig and colleague H.P. Kaufmann developed new paper chromatography techniques to identify and quantify fatty acids and documented the differences in fatty acid profiles in the blood samples of healthy and sick individuals [4,5] making her one of the first scientists to question the health implications of fat consumption [6].

Modifying the type of dietary fat became the foundation for the development of the Budwig Diet [6]. She believed that patients with cancer required highly unsaturated fatty acids (HUFAs now referred to as PUFA's or polyunsaturated fatty acids), to act as raw materials for cell membrane formation and to drive cellular respiration [4]. Diets lacking these fatty acids offered limited substrate for reactions and resulted in an oxygen poor environment, impeding cellular metabolism. She believed that processed fats, such as hydrogenated fats were oxygen inert and therefore, they have to be avoided [6]. Flaxseed oil, a key component of Budwig's diet which contains more amounts of polyunsaturated fatty acids (18–20% LA, 58–60% LNA) and lesser amounts of saturated and monounsaturated fat [7].

Interpretating Budwig's findings with latest research findings

In continuation of Warberg's findings that the deficiency of oxygen supply to cells below some critical level leads to cancer cell formation, Budwig further extended the concept by finding out the causative factors that lead to low oxygen supply. She was the first scientist to establish the relationship between the fatty acids and oxygen supply to the cells by way of incorporating the former in the cell membrane. The fatty acid she meant was the PUFA.

She focused her research on the development of cancer as a consequence of an aberration of cellular respiration, that in the absence of sulphydryl groups and/or a fatty acid partner, a low oxygen environment would be produced that would encourage cancerous cells to proliferate [4]. This finding is very important as it is the fundamental factor for the formation and proliferation of the cancer cells. It is established in science that both sulphydryl group and Fatty acids are present in the cell membrane [8,9]. Their role in cellular respiration has to be analysed discussed individually.

Role of USFA (PUFA) and SFA

Regarding the role of PUFA in oxygen supply, the studies of Cartwright, et al. [10] and Katan, et al. [11] establish that the PUFA from the diet is absorbed and incorporated in the erythrocyte membrane. This makes the cell membrane more fluid and thereby create deformability. As a result, the erythrocytes are able to carry oxygen more efficiently and supply to the tissue [12]. On the other hand, more incorporation of saturated fatty acids and decrease in the proportion of long-chain PUFA in cell membranes has been observed to make the cell more rigid thereby the oxygen transporting capacity is lowered leading to hypoxia [9]. The de-oxygenating role of adulterated and improper ratios of polyunsaturated fatty acids when incorporated into cell membranes is discussed by Brian S, et al. [13]. All these scientific reports support the Budwig's findings on the role of Unsaturated Fatty Acid (USFA)and Saturated Fatty Acid (SFA) in cancer cells in cellular respiration.

Role of Sulfhydryl group

Next theory of Budwig to be analysed is the role of sulfhydryl groups, thiols present in the cottage cheese. Budwig believed that sulfhydryl compounds were important to cellular metabolism, and in particular cellular respiration [4]. Recent studies indicate that, the thiol being a part of the cysteine residues in peptides and proteins, is known to play extremely important roles in several aspects of cellular function [14]. The importance of S atom of cysteine amino acid (a thiol group in cottage cheese) is revealed from its critical role in the formation of S-nitrosylation (SNO) enzyme of haemoglobin. This S-nitrosylation is a key mechanism for how red blood cells transport and deliver nitric oxide throughout the body, linking oxygen levels to the regulation of blood flow. Haemoglobin formation and release of SNO is a critical mediator of hypoxic autoregulation of blood flow in tissues leading to oxygen delivery [15]. These findings strengthen presumption of Budwig that the S in Thiol is involved in cellular respiration by involving in oxygen transport by haemoglobin.

Molecular Mechanisms

The next concept to be explained is the molecular mechanism through which the hypoxia condition makes the normal cells cancerous. Although Budwig could not able to explain the molecular mechanisms, recent studies have begun to highlight the diverse mechanisms by which hypoxia and HIF-dependent signalling promote cancer cell formation and progression [16-19]. Consequently, how oxygenation of tumour microenvironment weakens the impacts of hypaxial conditions and helps to improve cancer immunotherapy are discussed by Hatfield SM, et al., [20-22]. All the above research reports support the Budwig's concept of initiation and growth of cancer due to low oxygen supply to the cells.

In addition to involving in oxygen transport system, thiol is said to involve in anticancer mechanism by increasing the viability of anti-tumour CD8+ T cell populations by showing its higher presence. Thiol-high T cells persisted longer *in vivo* and exerted superior tumour control [23]. Thus, thiol's role in anticancer function may be considered far higher than what Budwig believed.

Dalzoppo D, et al. [24] have summarised the current structural and pharmacological knowledge in the field of thiol-activated anticancer agents, with a focus on the mechanism of their activation. Thus, it is evident that the thiol in the cottage cheese has many anticancer properties in one or the other means which were not perceived by Budwig during her times.

Discussion

The increase in cancer incidence and mortality is challenging current cancer care delivery globally, disproportionally affecting low- and middle- income countries when it comes to receiving evidence-based cancer prevention, treatment, and palliative and survivorship care. Patients in low, middle-income countries often rely on traditional, complementary, and integrative medicine that is more familiar, less costly, and widely available [25]. Under such condition there is a need to develop more evidence based traditional, complementary, and integrative medicine interventions to address these problems [26].

Evidence-based medicine uses the scientific method to organize and apply current data to improve healthcare decisions. Thus, the best available science is combined with the healthcare professional's clinical experience and the patient's values to arrive at the best medical decision for the patient [27,28].

The popularity of the Budwig diet protocol as an evidence-based therapy lies in the best scientific support that it processes and wide practice. On perusal of recent scientific study reports, Budwig's formula has got high scientific strength and evidences to treat it as one of the best evidence-based medicines for cancer prevention and control. The scientific strength involves peer reviewed international Journals' reports regarding wide applications, molecular mechanisms, clinical trials etc. of the constituents of the products used in the therapy. Here we analyse and discuss the various scientific strengths which supports the therapeutic values of Budwig diet protocol.

The basic strength of Budwig's therapy is her findings on the importance of Fatty Acids and sulphur containing thiols found in the diet. It was Budwig's theory that when the highly unsaturated fatty acids of flaxseed oil interacted with sulfhydryl groups from cottage cheese, the stored energy in the fatty acids would be released remedying the oxygen poor environment [4]. Although the mechanism she explained seems to be unscientific, recent scientific reports reveal that both UFA and sulfhydryl groups do involve in enriching the oxygen supply to the tissues by different means and deficiency of which led to hypoxia [29,30]. She may be the very first Scientist who related the occurrence cancer with lack of essential fatty acids and the thiol group in the diet. In the 1960ies during Budwig times, science was not in advanced level and many of her findings and theories could not be tested and established by scientific reports. However, she was able to predict the role of Fatty acids and thiols in cancer prevention by treating hundreds of cancer patients with her diet formula.

Modifying the type of dietary fat became the foundation for the development of the Budwig Diet [6]. Now, the recent research findings have recognized importance of Fatty Acid-Based Food and Nutraceuticals as Supporting Therapy in Cancer [31].

Another pioneer finding of Budwig, the role of fatty acids in the cell membrane as the key factor to be considered in cancer therapy, has now got a very strong support from many recent research findings [32-35]. In continuation of Budwig's findings, modern cancer therapy started focusing on cell membrane lipid-based therapies such as, membrane-lipid therapy [36,37] and lipidomic therapy [38].

Supporting the findings of the Noble Prize Laurate, Otto Warburg, Budwig strongly believed that low oxygen environment, hypoxia, is root cause for the origin and growth of cancer cells [4]. In support of this, many recent research findings put hypoxia as the fundamental factor for initiation, growth and spread of cancer cells [39-42]. These research findings explain various molecular mechanism that follow hypoxia resulting in cancer cell formation, growth, metastasis and resistance to therapy (Figure 1). Following these molecular mechanisms, new treatment strategies have been developed for combating the effects of hypoxia.

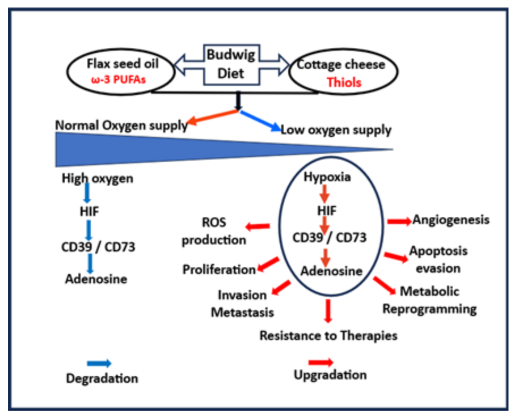

Figure 1: Role of omega 3 PUFAs and Thiols in Budwig diet in controlling Cancer. Deficiency of omega 3 PUFAs and Thiols in diet leads to low oxygen supply to the cells. This creates hypoxia condition in cell microenvironment leading to transformation of normal cells to cancer cells. Persistent hypoxia conditions encourage cancer cells to grow and spread to other organs by reprograming different metabolic process. More oxygen supply reverses the hypoxia condition.

Hypoxia and oxidative stress are core hallmarks of solid tumors and activated HIFs and NRF2 play pivotal roles in tumour growth and progression [43]. They recently, explored the elaborate interplay between HIFs and NRF2, providing insights into the significance of these interactions for the development of novel cancer treatment strategies. Herrera-Campos AB, et al. [44] and Anirudh Sattiraju, et al. [45] have explained and reviewed the molecular mechanism involved in the inhibition of immune system in cancer micro environment by hypoxia. As hypoxia stimulates the production of adenosine which is responsible for immunosuppression by inhibiting infiltration by antitumor T cells into the TME, supplemental oxygenation of TME will reverse the process and thereby antitumor immunity is enhanced [46,47].

Preventing the origin of cancer cells was the primary concern of Budwig. The molecular mechanisms which lead to initiation of tumour starts with cellular level oxidative stress due to constant free radical production and failure of counter balancing antioxidant system. Recent findings that relate oxidative stress to cancer-associated conditions are reviewed by Visconti R, Grieco D, [48], Reuter S, et al. [49] and Zhou Nj, et al, [50]. Additionally, oxidative stress plays a significant role in the initiation and development of cancer by causing DNA damage, disrupting apoptosis mechanisms, and promoting immune evasion [50]. Thus, it is imperative to combat oxidative stress which is the first step in cancer prevention. Ulrich K, and Jakob U. [51] highlighted the importance of Thiol-based redox systems that control the constant threat of molecular oxygen-mediated ROS production and damage. Soszyński M, and Bartosz G. [52] reported that decrease in accessible thiols as an index of oxidative damage to membrane proteins. Further, the role and mechanisms of 3-n- PUFA in combating oxidative stress and inflammation have been explained in detail [53,54]. Thus, it is evident that both PUFAs and Thiols present in Budwig Diet perform important roles in preventing initiation and formation of cancer cells (Figure 2).

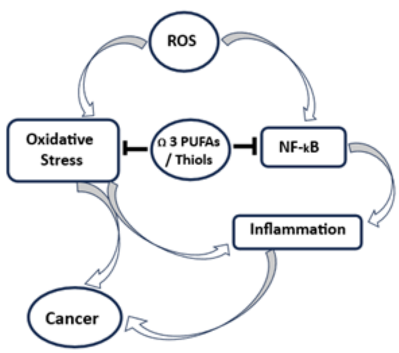

Figure 2: PUFAs and Thiols present in the Budwig Diet perform important roles in preventing initiation and formation of cancer cells.

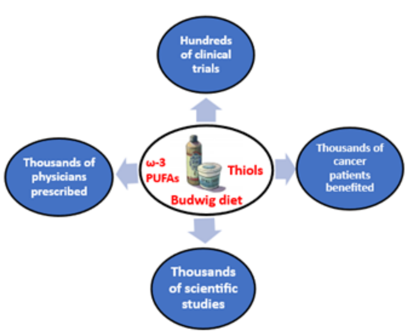

Figure 3: Justifications for considering the Budwig Diet as an effective Evidence based anticancer therapy.

There are number of literatures that highlight how the dietary consumption of the flax seed oil helps in cancer prevention. Several studies reported the cytotoxic effect of flaxseed oil against various types of cancer cells [55- 66]. A detailed account of role of Alpha-linolenic acid (ALA) in flax seed oil in chemo prevention has been reviewed by Roy et al., [67]. Recently, Al-Madhagy S, et al., [68] have provided a comprehensive review of the health benefits of flaxseed oil in relation to its chemical composition and comparison with other omega-3-rich oils highlighting its superiority over other oils in cancer prevention. They further reported the various research studies which explain flax seed oil's independent chemo preventive role against cancer and also its complementary roles with some conventional anticancer chemotherapy drugs.

Very recently, the collective mechanisms through which ω-3 PUFAs may function as both chemotherapeutic and chemo preventive agents in breast cancer have been dealt in detail by Marchio, et al. [69]. They also cited 43 references for using ω-3 PUFAs in clinical trials involving breast cancer. In the last decade, a large number of new clinical trials are being conducted to validate the effectiveness of ω3 PUFA in cancer therapy [70].

Apart from PUFA, another natural peptides linusorbs, occurring in flaxseed oil is said to exert cytotoxic effect on the Brain cancer, glioblastoma [60].

Anti-cancer property of yet another component of the Flax seed oil, the oleic acid (monounsaturated fatty acid), which constitutes about 20%, has also been recently explained by Deng B, et al. [71] in Endometrial cancer. Thus, the anticancer properties of the Budwig diet have got far greater values than what Budwig presumed and reported during her period and, these may be considered as the value additions to the Budwig diet in cancer treatment.

Conclusion

Evidence-based medicine (EBM) uses the scientific method to organize and apply current data to improve healthcare decisions. The best medical decision for the patient involves the best available science is combined with the healthcare professional's clinical experience and the patient's values. This is what needed for the success of any evidence-based medicine. Here, the best available science is emphasised for qualifying any medicine as an EBM. The best available science includes various clinical trials also. In this connection, presently hundreds of clinical trials are going on testing the role of ω3 PUFA in cancer therapy and thousands of people practice Budwig diet as a cancer therapy. Recent estimate reveals that the number of recent scientific publications relating omega-3 fatty acids to anti-cancer properties is in the thousands, with hundreds appearing each year. With all these facts, the Budwig Diet deserves to be recognized as an effective EBM for preventing and treating all types of cancers (Figure 3).

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