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Toxic chemotherapeutic nutrition of cancer cells by alkaline glucosodiene molecules via targeting metabolic of cancerous tumors: a promising theory for cancer treatment

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Author contributions

Maher Monir. Akl is responsible for the study design, data collection and analysis, and drafting of the manuscript, including writing the practical section and corresponding with other researchers. Amoura Mohammed. Abou El Naga is responsible for the direction and management of research projects. All authors have read and agreed to the final manuscript.

Competing interests

The authors declare no conflicts of interest.

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Abstract

Cancer is a genetic disease characterized by heritable defects in cellular regulatory mechanisms. Tumor cells must adapt their metabolism to survive and proliferate in the challenging conditions of the tumor microenvironment. To maintain uncontrolled cellular growth and survival, cancer cells alter their metabolism, which makes them dependent on a steady supply of nutrients and energy. Almost a century ago, the Warburg theory suggested that cancer cells consume glucose even in the presence of oxygen. Recent studies have confirmed that cancer cells indeed consume significantly more glucose than normal cells. Cancerous tumors require an acidic microenvironment with low oxygen levels for growth and spread. However, recent advances in pH measurement have shown that the intracellular pH of cancer cells is neutral or slightly alkaline compared to normal tissue cells. This finding indicates that not all tumors are highly acidic. Taking advantage of cancer cells' high glucose consumption, a strategy to lyse cancer cells is tested by means of glucose modifications that exploit the characteristics of their uncontrolled growth process. From the study of the molecular structure to give him alkaline properties that enable him to make defects in the tumor structure and possibly achieve cell killing, this situation will have a killing effect on cancer cells if small molecules of toxic atoms (alkaline atoms) can be continuously supplied to them through food, due to the uncontrolled consumption of glucose molecules by cancer cells. This theory attempts to investigate by changing the atomic structure of glucose molecules to make them alkaline glucosodiene molecules as one of the methods to kill cancer cells. By preparing alkaline glucosodiene molecules and performing animal experiments and histological observations, it was shown that tumors without alkaline treatment showed a tendency to infiltrate and grow, while tumors treated with glucosodiene molecules showed complete disappearance of cell structure and nucleolysis, supporting the validity of the theory.

Keywords: glucosodiene theory; cancer cell dissoluted; alkaline glucosodiene molecules

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Background

Cancer is a deadly disease that caused 8.8 million deaths in 2015–2018, accounting for 17% of all fatalities [1, 2]. Extensive research has been conducted to understand the biology and characteristics of cancer to develop successful clinical treatments. The pH levels of extracellular and intracellular tissues play a crucial role in the genesis and therapy of cancer. The extracellular pH (pHe) regulates human T cell proliferation and interleukin-2 receptor expression [3]. It is generally accepted that cancer cells have a higher pHe than normal cells [4, 5]. The pHe of normal tissues such as brain and subcutaneous tissues is usually in the range of 7.2–7.5, while the pHe of tumour cells is moderately acidic, ranging from 6.4 to 7.0. The fermentation process in tumours may affect pHe and pHi [6]. Therefore, from the 1930s through the 1980s, it was considered that pHe and pHi in cancer cells should be more acidic than those in normal cells [6, 7]. With the advancement of sensing technologies, several techniques have been developed to measure pHi and pHe in cancer cells, including pH-sensitive nuclear magnetic resonance spectroscopy, positron emission tomography radiotracers, magnetic resonance imaging, and optical imaging [8]. Recent findings suggest that the pHi of cancer cells is mildly alkaline or near neutral, similar to normal cells. This challenges the long-held belief that cancer cells have a higher pHi than normal ones [9, 10]. Researchers have investigated the mechanisms of pH control in cancer cells and microenvironments, and numerous membrane transporters across tumour cells have been found to maintain pH homeostasis in cancer cells. These transporters have been further used to manipulate pHe and pHi [11, 12].

Unique methodologies have been developed to alter the pHe/pHi ratio in cancer microenvironments and cells, inducing cancer cell apoptosis and increasing therapy efficiency [13]. Studies on the mechanisms of cancer-related metabolic changes have revealed a significant relationship between several pathways in human metabolism and malignant transformation [14–16]. Carcinogenesis is a multistep process that requires the removal of various cell-imposed obstacles, such as anti-proliferative responses, programmed cell death-inducing mechanisms, and senescence, which are usually caused by genetic changes in oncogenes and tumour suppressor genes [17]. The immune system is constantly activated to prevent tumour growth, leading to increased energy demand and a continuous supply of energetic substrates such as glucose [18]. The citric acid cycle, which converts glucose into CO_2 and H_2O, is a significant source of energy and is essential for the creation of adenosine triphosphate, a component of DNA, ribonucleic acid and phospholipids.

Glucose is essential for the pentose phosphate pathway and the production of reducing molecules such as NADPH. In advanced tumor cells, energy metabolism is significantly impaired due to symptoms such as nausea, anorexia and vomiting during disease progression. These symptoms prevent normal nutrition and thus the regular supply of carbohydrates, proteins, amino acids and vitamins. Reduced oral intake, resulting from anorexia or gastrointestinal obstruction, is critical in the development of the cancer cachexia syndrome. Significant changes in energy metabolism and biochemical/metabolic abnormalities in carbohydrate, protein, and lipid biochemistry and metabolism have been found, which may explain cancer-related anorexia/cachexia syndrome [19]. Cancer cells have altered energy metabolism, including increased resting energy consumption as well as increased sugar, lipid and protein metabolism. These changes result from cancer-related alterations in intermediate metabolism (carbohydrate, protein and lipids). Additionally, oncogene activation and tumour suppressor gene deactivation have been linked to cancer-associated metabolic remodeling of epigenetic markers [20]. The extracellular pH of tumour tissues (pHe) is often acidic and acidic metabolites, such as lactic acid, induced by anaerobic glycolysis in hypoxia, appear to be the main cause [21]. These conclusions were first proposed more than a century ago when Otto Warburg described the commonalities between several cancers, which are still under intense study [22]. Cancer cells have acquired the ability to be voracious glucose consumers with a rapid multiplication rate, with several cell signalling pathways ready to support this rapid expansion. Studies have shown that calorie restriction and food deprivation may be cancer protective and improve treatment response [23–25]. However, lowering glucose levels may limit the metabolic flexibility of these cells under stress. Thus, metabolically targeting cancer is an intriguing area of research, and recent studies have explored the efficacy of metabolic medicines for cancer treatment. The major challenge in targeting cancer cells in the body is that they have the same structure and growth process as any other cell in the body. They are not subject to the body's cell life cycle and activity system, as they lack self-killing elements or procedures. One strategy for dissolving cancer cells is to exploit the unregulated growth process of cancer cells through glucose modification. This theory examines the atomic structure of glucose molecules by changing them to give them alkaline qualities to kill cancer cells. By continuously providing small molecules of toxic atoms (alkaline atoms) to cancer cells through food consumption, we aim to create a defect in tumor structure that may lead to cauterization of a cell. The sucrose (sugar) molecule has 22 hydrogen atoms that surround the oxygen, and the carbon atoms are connected to two rings, one of fructose and the other of glucose. Glucose is the primary source of sustenance for body cells, including cancer cells. This is a promising hypothesis for cancer treatment that requires further investigation.

The effects of hypoxia on glucose utilization in tumors

The availability of growth factors regulates proper cell proliferation in tissues as well as interactions with surrounding cells. The availability of nutrients and oxygen, which are required for cell proliferation and metabolism, is heavily reliant on blood flow. The development of new blood vessels does not occur during the first tumour growth. Tumour cells circumvent environmental growth restrictions (Figure 1). This is accomplished through the acquisition of the ability to proliferate independently of growth signals, as a result of mutations in receptor-associated signalling molecules, and by becoming hypersensitive to antigrowth stimuli, such as those mediated by cell-to-cell interactions.

Uncontrolled cell proliferation in the early stages of carcinogenesis drives tumour cells away from blood arteries and hence from oxygen and nutrition supplies.

Only diffusion across the basement membrane and via the peripheral tumor-cell layers allows oxygen and glucose to enter the

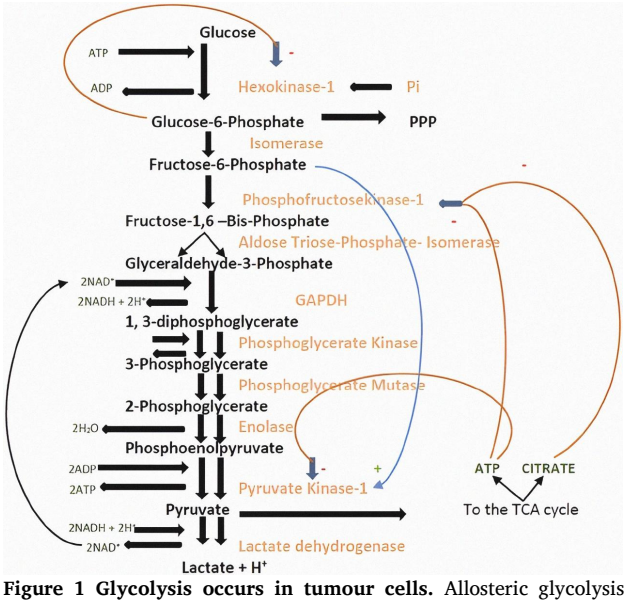

Figure 1 Glycolysis occurs in tumour cells. Allosteric glycolysis modulation confers metabolic flexibility in relation to local pO2.

core cells of a non-vascularized tumour. However, 100 mm away from blood arteries, partial oxygen pressure drops to extremely low levels.

Hypothesis

Glucose has the potential to serve as a suitable vector for carrying toxic substances to cancer cells due to the fact that all cells in the body, including cancer cells, rely on glucose molecules for their growth and energy production. It can be achieved by replacing some of the hydrogen tentacles in the sucrose molecule with alkali elements like sodium. This substitution is possible because hydrogen and other first-rank raw elements in the periodic table share the same atomic structure of having one electron in the valence band of atomic electron orbit. It is hypothesized that cancer cells may not be able to differentiate between pure glucose and glucose in which some of its hydrogen tentacles have been replaced by other alkali atoms. This substitution can result in the creation of highly toxic deterging properties of hydroxide alkali molecules when they come into contact with water molecules, such as NaOH and KOH. Consequently, cancer cells that unintentionally consume alkali atom-ridden glucose molecules dissolve uncontrollably.

Alkali atoms are used to replace some of the glucose hydrogen tentacles

Due to the presence of 22 tentacles in each hydrogen atom (Figure 2), it is feasible to replace sucrose molecules with any atomic element in the first row of the periodic table. This replacement process is exothermic and easy to execute since the first-row elements have lower ionization energies compared to hydrogen. Moreover, by substituting a few hydrogen atomic tentacles in glucose with alkali elements like sodium, potassium, or cesium, glucosodiene molecules can become toxic to cells that consume them. For instance, when sodium replaces hydrogen, the glucose ring of the sucrosodiene molecule becomes highly corrosive due to the strong nature of the first-row elements. The technique of substituting hydrogen atomic tentacles in glucose with alkali elements, such as sodium, potassium, or cesium, guarantees one-to-one atomic replacement because these alkali atoms have only one valence electron in their outermost electronic orbital, similar to hydrogen. Alkali atoms are located in the first row of the periodic table. It is noteworthy that hydrogen atoms contain two valence electrons in their S orbital, but only one electron in an isolated hydrogen atom. Two hydrogen atoms typically share electrons in both S orbitals to form a stable electronic configuration of a valence bond, which is a hydrogen molecule [26, 27].

The valence electron in the outermost orbital is a shared chemical feature of hydrogen and alkali elements. Hydrogen atoms in a molecule can be replaced one for one with other alkali elements (Figure 3), without significantly altering the molecule's structure. Glucose and glucosodiene have similar molecular structures and chemical characteristics. (Figure 4) If cancer cells can distinguish between pure glucose and alkali-replaced glucose molecules, then substituting alkali elements for glucose will not be effective. However, if cancer cells cannot distinguish between the two, they may mistakenly take in sodium-replaced glucose molecules as sustenance.

Methods

The exothermic replacement of hydrogen with sodium in sucrose molecules can be facilitated by boiling a mixture of sugar and sodium bicarbonate dissolved in water, which produces abundant carbon dioxide bubbles. To prepare the solution, mix 5 grams of food-grade sodium bicarbonate and 5 grams of glucose in 100 milliliters of reverse osmosis filtered water. The solution is boiled at medium heat or highest heat setting for about 20 minutes. The resulting solution has a slightly bitter, sweet taste, which is critical for tricking cancer cells into absorbing glucosodyne molecules. This solution can be lyophilized to produce a powder of alkaline glucosodyne molecules, which can target and treat cancerous tumors, especially solid tumors, as a therapeutic supplement.

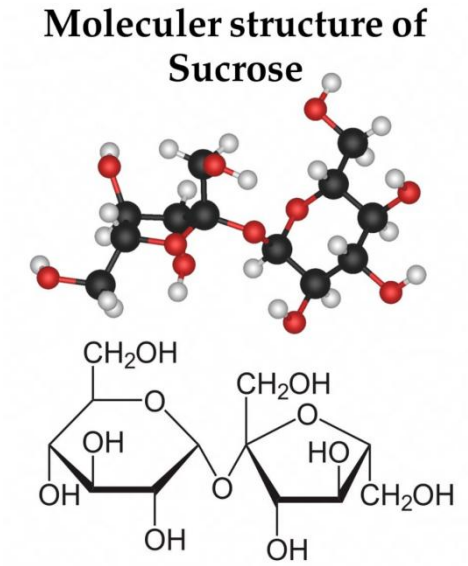

Figure 2 The sucrose (sugar) molecule's molecular structure. The sucrose molecule is composed of two rings, one of fructose and the other of glucose, with 22 surrounding hydrogen atoms around the oxygen. Glucose is a primary nutritional source that supplies energy to body cells including cancer cells.

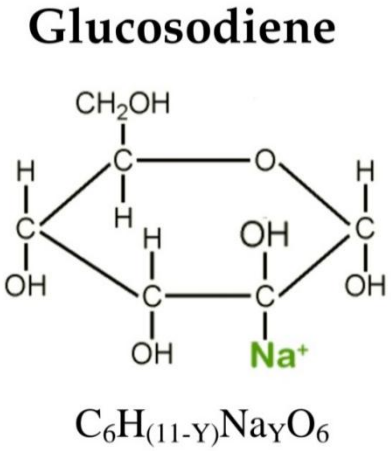

Figure 3 Structure of glucosodiene molecule. This is if one atom of hydrogen is replaced by one atom of sodium.

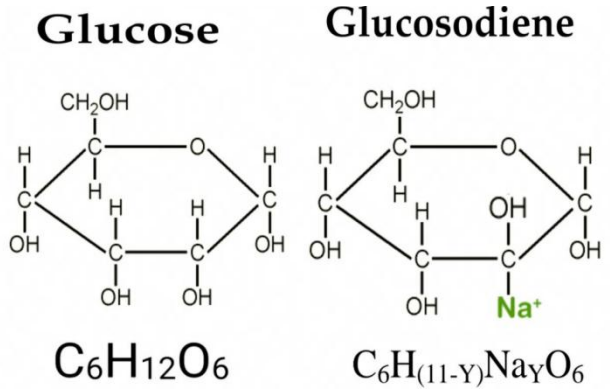

Figure 4 The difference in molecular structure between glucose molecule and the glucosodiene molecule. Which cancer cells are unable to differentiate from pure glucose because they lack the necessary brain functions.

Evaluation the effect of theory in an initial application on breast cancer cell models (EMT6 cell line) in vitro and in vivo tumor-bearing animal model as a short communication intended to support the theory

Cell line

The EMT6 breast tumor cell line (purchased from Pharmaceutical Research Center, National Research Center, Dokki, Egypt) was cultured in RPMI 1640 medium supplemented with 10% fetal calf serum plus penicillin/streptomycin in humidified air with 5% CO_2–95% envelope. Atmospheric at 37 ˚C. For cytotoxicity studies with a solution of glucosodiene molecules, the cells were grown in 30 mm culture dishes.

Assessment cytotoxicity

The EMT6 cell line was grown to the confluence of cultured dishes 30 mm in diameter. Each dish contains three milliliters of medium. 400 mol 0.1 mol/L glucosodiene solutions (pH = 9) were added to the media for the glucosodiene solution treatment group, and the culture dishes were put on an ultra-clean bench for 1 hour. There was no treatment for the control group. Following therapy, the media was aspirated and new media was applied to the cells. They were then incubated at 37 ˚C for a further 18 hours. After 18 hours, the medium was aspirated, the cells were washed with phosphate-buffered saline, and the cells were trypsin zed from the culture dishes. During moderate vortexing, the cell pellet was re-suspended. Cell viability was determined by introducing 100 uL of re-suspended cells into the CASY cell counter system (Model TTC, CASY® Technology, Berlin, Germany), and the cell diameter distribution and vitality were determined using its analyzer system. Every experiment was carried out in triplicate.

In vivo tumor-bearing animal model

Animal studies were conducted in line with the International Convention on the Care of Laboratory Animals. The ethical approval unit is Mansura University Faculty of Science Ethics committee and the approval number is Sci-Z-P-2023-123. EMT6 tumour cells were cultured in RPMI 1640 media before being extracted, washed, and resuspended in sterile phosphate-buffered saline. In oxidizers from female BALB/c mice (6–8 weeks old), 0.2 mL of EMT6 tumour solution was injected. The tumours in the donor rat bull were removed under sterile conditions and chopped into 1 mm cubes when they reached their greatest size of 1.0–1.5 cm. Tumour cells were re-suspended after being ground and filtered. A 0.2 mL solution was injected into the right oxter of four BALB/c female mice weighing 15–20 g. After ten days, these four mice with tumours ranging in size from 1.0 to 1.5 cm were randomly assigned to one of two groups. In the control group, two mice received no therapy. Two more mice were given 1.5 mL of a solution of alkaline glucosodiene molecules (1 mol/L, pH = 9) orally. Tumour size was measured daily following treatment in each group using the Carlsson formula: V = 1/2 a b 2, where an is the longest diameter (mm) and b is the smallest diameter (mm).

The statistical analysis

The t-test was used to identify differences between experimental groups (with in vitro cell studies performed in triplicate). A statistically significant difference between groups was defined as $P < 0.05$.

Cytotoxicity comparison of cancer cells in vitro

On a breast tumour cell line, we investigated the cytotoxicity of cancer cells using a solution of glucosodiene molecules. The CASY analyzer system revealed that the cell viability of the control group, the 0.1 mol/L glucosodiene molecules solution treatment group, and the treatment group were all viable, (56.17 ± 11.29%) the control group's cell viability, (86.5 ± 4.28%) (Figure 5).

Histological evaluations

Tumor tissues at the treatment location were killed and histologically evaluated by light microscopy immediately after treatment in four mice. This explains how the accumulation of sodium molecules combined with glucose molecules breaks down the tumor inside the disease model. Once the cancerous tumor consumes them, the glucose molecules disintegrate, and the sodium molecules combine with the hydroxide molecules inside the tumor infrastructure to form sodium hydroxide, causing cauterization and collapse. The tumor is shown in the histology model. Tumors were cut into 5-mol frozen sections and stained with hematoxylin and eosin for histological examination. Untreated tumors showed a trend of infiltrative growth (Figure 6A). The tumors treated with glucosodiene molecules showed complete disappearance of the cell structure and nucleolysis (Figure 6B), which supports the validity of the theory as a first step in the applied theory.

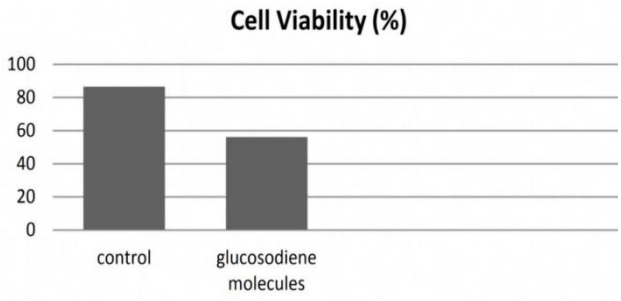

Figure 5 In vitro EMT6 breast cell survival of the control group, glucosodiene molecules, respectively. The data represent the mean standard error of the mean for triple experiments. The viability of glucosodyne molecules differs dramatically from that of the control group.

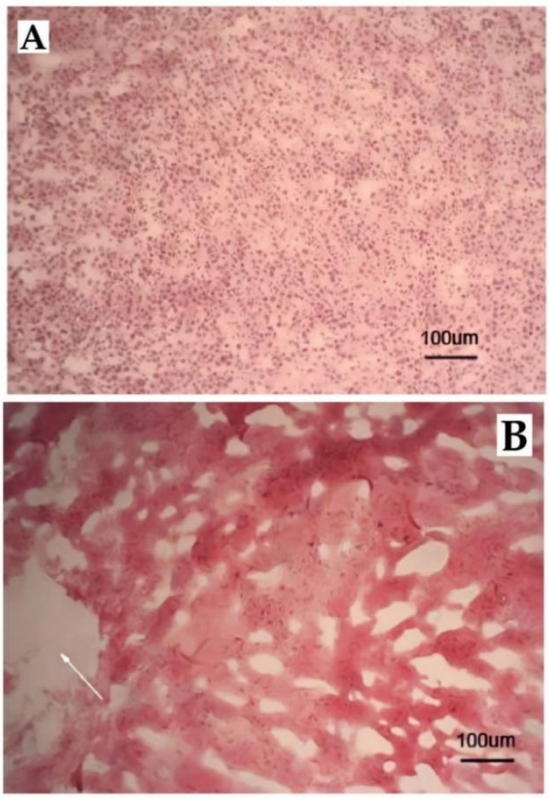

Figure 6 An EMT6 tumour was stained with hematoxylin and eosin immediately after treatment for the treatment and control groups, respectively. (A) Infiltrator growth was observed in the control group. (B) A group of glucosodiene molecules with a white arrow indicating the area of cell breakdown caused by sodium activity and necrosis around the injection site.

Evaluation the effect of glucosodiene's on normal cells

Glucosodiene-induced cancer cell breakdown may affect healthy cells, which undergo natural death to regenerate. However, this occurrence is more widespread in normal cells than in isolated cancer cells. Glucosodiene may hasten the death of aging cells, which resist elimination. The breakdown of sugar molecules without oxygen causes acid, but discomfort subsides when cells take up glucosodiene. The body's T cells eliminate any remaining cancer cells after recovery [28]. Normal cells can regulate their natural alkalinity and excrete excess pH [29, 30]. This could be a significant development in chemotherapy, with fewer side effects than conventional drugs. Further research is required.

Molecular chemical formulas for sucrose variable molecules predicted for compounds intended for cancer therapy

It is scientifically feasible to anticipate similar results by substituting hydrogen atoms in glucose molecules with other heavier alkali elements. All alkali elements in the periodic table possess the same chemical properties as sodium, enabling them to replace hydrogen atoms on a one-for-one basis without disturbing the primary structure of the target molecules. The ability of atoms to form chemical bonds depends on the number of outermost electrons in their shell structure. Additionally, different glucose molecules containing different alkali elements may respond differently based on the type of cancer present in the body, potentially leading to more effective cancer cell elimination. The solitary active valence electron in the outermost shell of alkali elements is present in every case. Therefore, we refer to the sucrose molecule modified by sodium as its scientific name, sucrosodiene. The nomenclature for potassium replacement is sucropotasiene, for cesium replacement is sucrocesiene, for rubidium replacement is sucrorubidiene, and for francium replacement is sucrofransiene. These are denoted chemically in Table 1. Similarly, the scientific name for a glucose molecule transformed by sodium is glucosodiene. The name for potassium replacement is glucopotasiene, for cesium replacement is glucocesiene, for rubidium replacement is glucorubidiene, and for francium replacement is glucofransiene. These are denoted in Table 2.

Discussion

Cancer cells are known to be more sensitive to heat and apoptosis than normal cells, and this property has been leveraged to develop glucosodiene molecules that induce tumor hyperthermia. The chemical mechanism of sodium processing in this approach is similar to the cathode reaction in electrochemotherapy. Cancer cells take up glucosodiene because they are capable of growing uncontrollably and lack the sophisticated brain function necessary to distinguish between glucose and modified glucose. Glucosodiene kills cancer cells by breaking down glucose molecules into carbon dioxide and water, generating energy that alkali elements utilize to dissolve cancer cells from within. This approach is effective for treating numerous types of cancer due to the uncontrolled development of cancer cells. The traditional approach of eliminating cancer cells is not applicable in this theory, as cancer cells are dissolved from within due to their uncontrollable consumption of glucose molecules. Cancer cells have an uncontrolled ability to multiply and consume glucose molecules. Glucosodiene molecules have been developed to exploit this characteristic by inducing tumor hyperthermia, which makes cancer cells more sensitive to heat and apoptosis. Glucosodiene breaks down glucose molecules into carbon dioxide and water, generating energy that is utilized by alkali elements to dissolve cancer cells from within. Cancer cells that consume sodium-laced glucose struggle to retain their rigid cell structure and instead disintegrate and dissolve into the bloodstream before being excreted as urine. This approach is particularly effective in treating numerous types of cancer because cancer cells predominantly grow in lumped form, allowing for a localized concentration of alkali elements. The theory proposed by Maher Akl targets cancerous tumors through their metabolic activity using alkaline glucosodiene molecules, and has the potential to pave the way for a new branch of chemotherapeutic sciences known as "toxinutromedicanical-chemotherapy". This innovative approach challenges the traditional notion of eliminating cancer cells, and instead proposes using a localized concentration of alkali elements to dissolve cancer cells from within.

Conclusions

The current theory proposes a method to eradicate cancer cells by exploiting their high demand for glucose molecules, which leads to a severe lack of nutrients necessary for the body. This method involves transforming glucose molecules using alkali elements (glucosodiene molecules), which have similar chemical properties due to having one valence electron in their outermost shell. This theory attempts to investigate by changing the atomic structure of glucose molecules to make them alkaline as one of the methods to kill cancer cells. By preparing alkaline glucose molecules and performing animal experiments and histological observations, it was shown that tumors without alkaline treatment showed a tendency to infiltrate and grow, while tumors treated with glucosodiene molecules showed complete disappearance of cell structure and nucleolysis, supporting the validity of the theory. The speed of recovery depends on the patient's cancer stage, as well as the natural chemical properties and interaction of the supplement within cells. Further research is needed to determine the optimal number (Y) of alkali elements in the modified glucose molecule to enhance its effectiveness in killing cancer cells, as cancer cells may recognize the modification. Although these chemicals are present in nature as food, their true medical characteristics remain unknown or unstudied.

Future perspectives

The manuscript proposes a new theory for treating cancer by targeting the metabolism of cancerous tumors with alkaline glucosodiene molecules. The theory aims to modify the atomic structure of glucose molecules, making them alkaline to exploit the uncontrolled growth process of cancer cells and cause defects in the tumor structure, ultimately leading to cell death. The effectiveness of this approach has been demonstrated through animal experiments and histological observations, which showed complete disappearance of cancer cell structure and nucleolysis following treatment with

Table 1 The compounds resulting from the modification of two sucrose molecules by adding alkaline elements

The compounds resulting from the modification of two sucrose molecules by adding alkaline elements	Chemical formulas
Sucrosodiene	$C_{12}H_{(22-X)}Na_XO_{11}$
Sucropotasiene	$C_{12}H_{(22-X)}K_XO_{11}$
Sucrocesiene	$C_{12}H_{(22-X)X}CsO_{11}$
Sucrorubidiene	$C_{12}H_{(22-X)}Ru_XO_{11}$
Sucrofransiene	$C_{12}H_{(22-X)}\ Fr_XO_{11}$

Table 2 The compounds produced by modifying the glucose molecule through the addition of alkaline elements

The compounds resulting from the modification of the glucose molecule by adding alkaline elements	Chemical formulas
Glucocesiene	$C_6H_{(11-Y)}Cs_YO_6$
Glucocesiene	$C_6H_{(11-Y)}Fr_YO_6$
Glucopotasiene	$C_6H_{(11-Y)}K_YO_6$
Glucorubidiene	$C_6H_{(11-Y)}Ru_YO_6$
Glucosodiene	$C_6H_{(11-Y)}Na_YO_6$

alkaline glucose molecules. These findings have important implications for the future treatment of cancer, and further research could lead to the development of a new class of chemotherapeutic agents that target cancer cell metabolism. The manuscript provides a solid foundation for future studies on the use of alkaline glucosodiene molecules for cancer therapy and paves the way for the development of new and effective cancer treatments that exploit the unique characteristics of cancer cell metabolism.

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