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# Developing the theory of toxic chemotherapeutic nutrition for cancer cells and targeting tumors via glucose mutation: Medical guidance and integrated therapeutic approach

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ABSTRACT

Cancer is a complex genetic disease characterized by aberrant cellular behaviors, including uncontrolled growth, invasion, and metastasis. The development of personalized treatment strategies based on genomic profiling has led to improved outcomes. Recent scientific endeavors have focused on targeting cancer through metabolic approaches, capitalizing on the altered metabolic pathways in cancer cells. Glucosodiene polymer, a newly derived compound from glucose, has shown promising results in inhibiting glucose metabolism and modifying the tumor's microenvironment acidity. The Maher Akl Theory "Glucose Mutation" proposes a strategic approach to target cancerous tumors by inhibiting glucose metabolism and altering the tumor's microenvironment acidity using glucose isomer polymers. The goal is to disrupt the metabolic activity of the tumor and potentially modify and control the disease. This manuscript provides an overview of the metabolic vulnerabilities of cancer cells, evaluates the synthesis and chemical structure of glucosodiene, documents its safety, and explores its potential as a targeted therapy for cancer treatment. Additionally, a subset of successful clinical trials is presented, focusing on a case of successful treatment of triple-negative breast cancer (TNBC) with glucosodiene, and Medical Guidance and Integrated Therapeutic Approach; The Protocol of Glucose Mutation Theory via Glucosodiene and indication of Positive Tumor Lysis Syndrome The potential mechanisms of action of glucosodiene in cancer, including its impact on glucose metabolism, modulation of signaling pathways, and immune-enhancing effects, are discussed.

**Keywords:** cancer, metabolism, glucose, glucosodiene targeted therapy, triple-negative breast cancer, tumor microenvironment, glucosodiene polymer structure, safety of glucosodiene, tumor lysis syndrome, GLP-1 agonists

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## INTRODUCTION

Cancer is a complex disease that has undergone evolving definitions over time. Initially, it was characterized as uncontrolled cell growth and proliferation [1]. However, recent advancements in cancer research have led to a more nuanced understanding. Nowadays, cancer is recognized as a genetic disease resulting from cellular regulatory defects, encompassing a range of disorders characterized by abnormal cell behaviors, including uncontrolled growth, invasion, and metastasis [2, 3]. This updated definition emphasizes the underlying genetic alterations and the diverse nature of cancer. The treatment of cancer involves various modalities, such as surgery, chemotherapy, radiation therapy, immunotherapy, and targeted therapy [4]. Each modality aims to eradicate or control cancer cells through different mechanisms. Surgery involves the physical removal of tumors, while chemotherapy utilizes cytotoxic drugs to kill rapidly dividing cells. Radiation therapy employs high-energy radiation to damage cancer cells' DNA, impairing their ability to replicate. Immunotherapy harnesses the body's immune system to recognize and eliminate cancer cells, and targeted therapy focuses on specific molecular targets within cancer cells [5]. Some of which may lead to an impact on the patient's life expectancy after treatment [6]. The efficacy of these treatment modalities varies depending on the cancer type, stage, and individual patient factors. Personalized treatment approaches based on genomic profiling are gaining prominence, allowing for tailored therapies with improved outcomes [7].

Recent scientific endeavors have focused on targeting cancer through metabolic approaches. One hallmark of cancer cells is their heightened glucose consumption compared to normal cells. Cancer cells rely on altered metabolic pathways, including aerobic glycolysis, to meet their energy demands and promote tumor growth [8]. The metabolic alterations lead to the accumulation of lactate and a decrease in pH, resulting in an acidic tumor microenvironment. Researchers are exploring strategies to exploit these metabolic vulnerabilities, including inhibiting glucose metabolism, disrupting energy production, and altering the tumor microenvironment's acidity [9]. These metabolic approaches offer promising avenues for targeted cancer therapy [10]. The glucolipotoxicity theory proposes that the accumulation of glycolipids within cells plays a fundamental role in the development of cancer. This theory builds upon the well-known Warburg effect, which describes the increased glucose uptake and

lactate production observed in cancer cells, even in the presence of oxygen. According to the glucolipotoxicity hypothesis, the closure of glucose transporters on cancer cell membranes is attributed to the excess accumulation of glycolipids, leading to disruptions in cellular homeostasis. This temporary closure halts glucose uptake, allowing the cell to metabolize the accumulated glucose before resuming normal glucose uptake. As a result, cancer cells engage in anaerobic glycolysis, breaking down glucose into lactate, even in the presence of oxygen. This metabolic shift results in the production of lactic acid, leading to an acidic microenvironment within the tumor. The acidic conditions not only promote tumor growth but also contribute to immune suppression, angiogenesis, and invasive behavior. The glucolipotoxicity theory provides a broader understanding of the primary causes of cancer by highlighting the interference of accumulated glycolipids with cellular processes and the activation of oncogenic pathways. These dysregulated metabolic processes and their effects cellular function are considered to be crucial drivers of tumor development. By elucidating the mechanisms underlying the Warburg effect and glycolipid metabolism dysregulation, the glucolipotoxicity theory offers valuable insights into the complex nature of cancer. This perspective contributes to the growing body of knowledge in the field and has the potential to pave the way for the development of innovative therapeutic strategies targeting the primary cause of cancer [11]. The Maher Akl Theory "Glucose Mutation", also known as "Toxic chemotherapeutic nutrition of cancer cells by alkaline glucosodiene molecules via targeting metabolic of cancerous tumors: a promising theory for cancer treatment," has been proposed as an innovative approach to target cancerous tumors, particularly those with solid or clustered growth patterns, by exploiting their metabolic activity. This theory encompasses the synthesis of glucose isomer molecules into glucose isomer polymers, which are specifically engineered to inhibit glucose metabolism within tumors by capitalizing on the alkaline properties of the polymers. Consequently, this impedes tumor growth and alters the hydrogen ion concentration within the tumor microenvironment.The primary objective of the Akl Theory is to disrupt the metabolic activity of the tumor, potentially leading to disease modification and control. In the initial phase of the theory's development, challenges arose regarding the lack of structural characterization of the glucose isomer polymer and the absence of testing on natural cells. In this study, we address these concerns by providing comprehensive chemical structural documentation and demonstrating the safety of the glucose isomer polymer on human cells. Furthermore, we discuss the clinical observations from the first serendipitous case of triple-negative breast cancer with bone metastasis that underwent treatment with the glucose isomer polymer. Additionally, it is important to note that our research elucidates the chemical structure and safety profile of the glucose isomer polymer, providing valuable insights into its potential therapeutic applications. We aim to contribute to the scientific community's understanding of this novel approach and its promising implications for the treatment of triple-negative breast cancer and other malignancies [12, 13].

## HYPOTHESIS

The heightened glucose consumption by cancer cells can be attributed to several mechanisms. Firstly, cancer cells often exhibit upregulated expression of glucose transporters, such as GLUT1, GLUT2, GLUT3 gates (Figure 1), and other variants, which facilitate increased glucose uptake into the tumor cells [14]. This heightened glucose uptake provides the necessary fuel for cancer cell growth and proliferation. As a consequence of this elevated glucose metabolism, cancer cells undergo glycolysis (Figure 2), a process that converts glucose into energy and produces large quantities of lactic acid. The accumulation of lactic acid results in the acidification of the tumor microenvironment [15]. This acidic environment plays a significant role in tumor progression and metastasis by promoting angiogenesis, immune evasion, (Figure 3) and tissue invasion [9, 16].

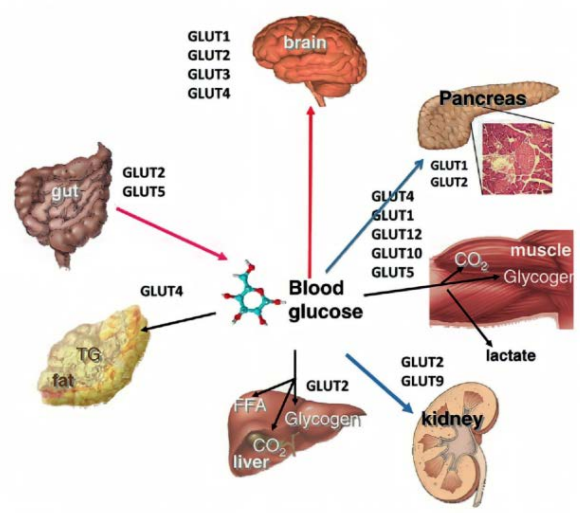


**Fig. 1.** The role of GLUTs glucose transporters in maintaining glucose homeostasis is vital in facilitate glucose transport across cell membranes, ensuring glucose balance in the body. The diversity of glucose receptors in different organs underscores their significance in biological contexts. Consequently, alterations in these receptors may contribute to tumor development in affected organs. In the context of cancer cells, heightened glucose consumption can be attributed to mechanisms including upregulated expression of glucose transporters like GLUT1, GLUT2, and GLUT3

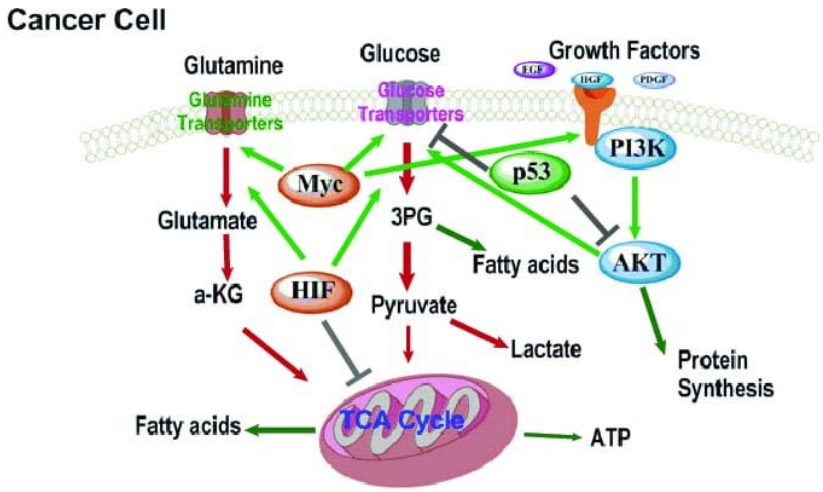


**Fig. 2.** Cancer cells exhibit a metabolic shift called glycolysis, characterized by increased reliance on the conversion of glucose to lactate, even in the presence of oxygen (the Warburg effect). This metabolic adaptation provides cancer cells with the energy and building blocks required for their rapid proliferation. Glycolysis involves the enzymatic conversion of glucose to pyruvate, resulting in ATP production and the generation of NADH. The up regulation of glycolytic enzymes facilitates this process. Understanding glycolysis in cancer cells is essential for developing targeted therapies to disrupt their metabolic dependencies and inhibit tumor growth

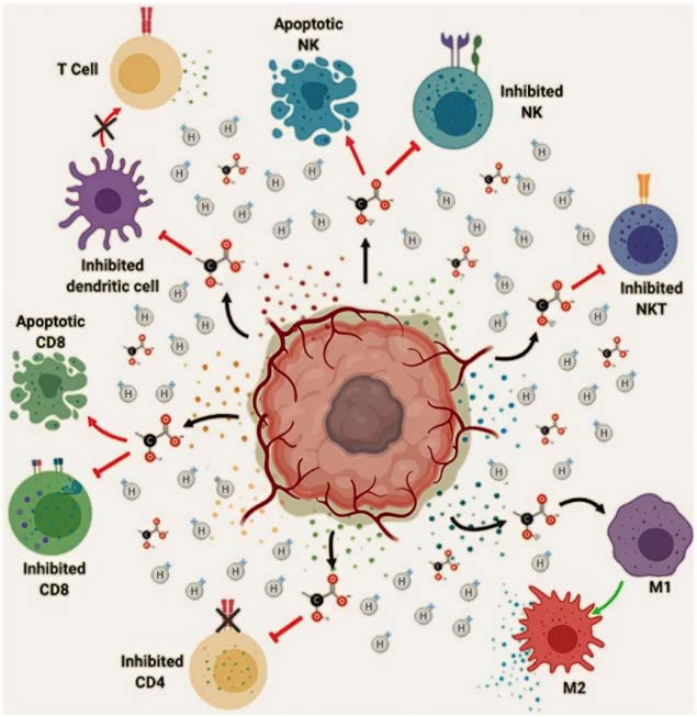


**Fig. 3.** The acidic tumor microenvironment, facilitated by lactate secretion, plays a significant role in tumor progression and metastasis. It inhibits immune cell activation and proliferation, induces apoptosis in specific immune cells, and promotes the polarization of macrophages towards a pro-tumorigenic phenotype. This leads to immune suppression, immune evasion, and favorable conditions for tumor growth, invasion, and migration

By capitalizing on the reliance of cancer cells on glucose, a potential therapeutic strategy involves introducing a chemical alteration or structural mutation to the glucose molecule, allowing it to enter the tumor as a polymer with alkaline properties. This modified glucose polymer may hinder glucose metabolism within the tumor and alter its acidic hydrogen environment, thereby impeding tumor growth, spread, and potentially inducing cell death. Moreover, glucose serves as an attractive target for combating various types and stages of cancer since most cancerous tumors heavily rely on glucose metabolism, a phenomenon known as the Warburg effect [17]. By targeting the metabolic activity of cancer cells and specifically their glucose receptors, it is possible to disrupt the tumor's nutrient supply and inhibit its growth. This can be accomplished by utilizing glucose as a carrier for delivering toxic substances directly to cancer cells or by inducing a structural mutation that imparts alkaline properties to glucose;

understanding the metabolic characteristics of cancer cells and their dependence on glucose metabolism provides valuable insights for developing innovative therapeutic approaches aimed at targeting tumor cells through their metabolic vulnerabilities [18].

## METHODS

The synthesis of glucosodiene in this study involved the utilization of dextrose monohydrate ($C_6H_{14}O_7$) and sodium bicarbonate ($NaHCO_3$) as starting materials. The method employed included the following steps: Accurately weigh 3.5 grams of dextrose monohydrate and 2.5 grams of sodium bicarbonate using a digital balance. Dissolve the measured quantities of dextrose monohydrate and sodium bicarbonate in 100 mL of sterile water. Gently stir the mixture to ensure even distribution. Apply heat to the mixture, raising its temperature to 100 degrees Celsius with the aid of a heating apparatus. Maintain this temperature for duration of five minutes. Monitor the reaction mixture closely for the formation of bubbles, indicating the release of carbon dioxide and confirming the progress of the reaction. Allow the reaction mixture to cool down to room temperature. Once cooled, the mixture can undergo further purification and characterization processes. It is worth noting that the purification and characterization procedures in this study involved subjecting the 100 mL solution to refrigerated drying, followed by the utilization of the resulting concentrate for subsequent bioassays. These processes ensure the removal of impurities and the preparation of a refined sample for further analysis. The synthesis methodology described above adheres to established chemical principles and techniques. However, to validate the purity, structure, and properties of the synthesized glucosodiene compound, it is imperative to conduct additional experiments and analyses. These would provide further insights into the compound's characteristics and enable a comprehensive evaluation of its potential applications.

## GLUCOSODIENE

Glucosodiene is a novel polymer compound synthesized through the reaction between dextrose and sodium bicarbonate. It is a polymer compound with a molecular formula of $C_{12}H_{22}O_{11}$. The synthesis of glucosodiene follows the scientific principle that elements with a common atomic structure, such as hydrogen and other first-row elements in the periodic table, share similar characteristics due to the presence of one electron in the valence shell. Glucosodiene is an isomer polymer of glucose and exhibits structural similarities to glucose. It is formed through the self-association of monomers derived from glucose isomers that are connected through 1-2 linkages. The molecular structure of glucosodiene is represented as (1-2-O-β-D-Glucopyranosyl-α-D-glucose) (Figure 4). The primary monomer responsible for the formation of the glucosodiene polymer is an isomer of glucose.

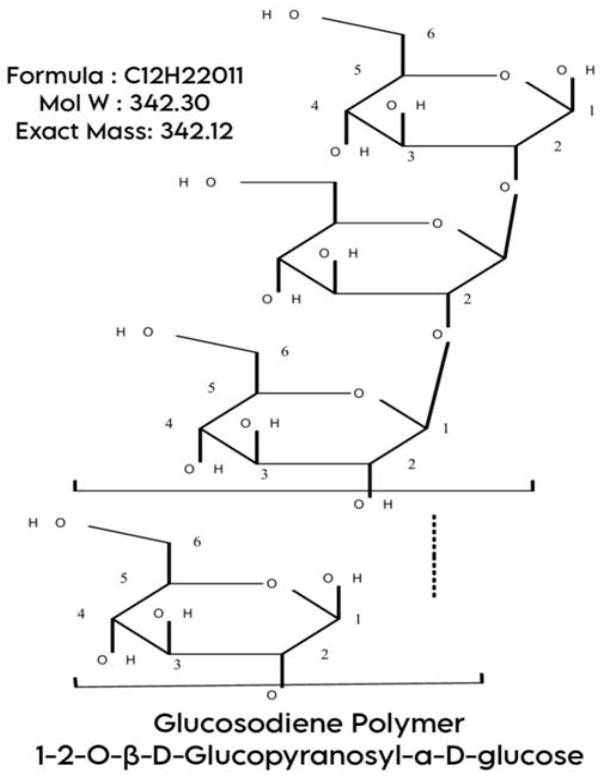


**Fig. 4.** The structural configuration of the glucosodiene polymer is composed of monomers derived from glucose isomers that are connected through 1-2 linkages. Its molecular structure is represented as (1-2-O-β-D-Glucopyranosyl-α-D-glucose). The primary monomer responsible for the formation of the glucosodiene polymer is glucose, with a molecular mass of 178.9 as determined by LC-MS results. Interestingly, this monomer shares a similar structural composition to trehalose but undergoes self-association through 1-2 linkages, resembling the molecular structure of sophorose

The synthesis of glucosodiene involves the reaction between dextrose and sodium bicarbonate in a heated mixture. The resulting polymer compound is then dried and subjected to NMR (Figure 5-7) and LC-MS analysis (Figure 8-11). The NMR analysis confirms the presence of the formula $C_{12}H_{22}O_{11}$, while the LC-MS analysis validates its identity as 1-2-O-β-D-Glucopyranosyl-α-D-glucose [18].

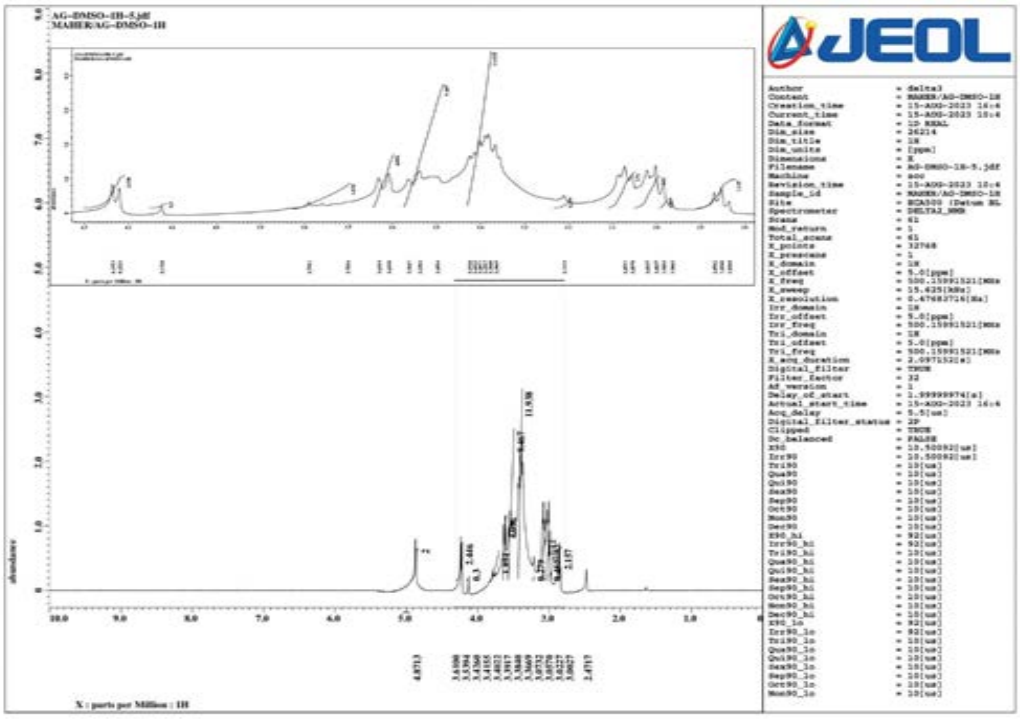

**Fig. 5.**

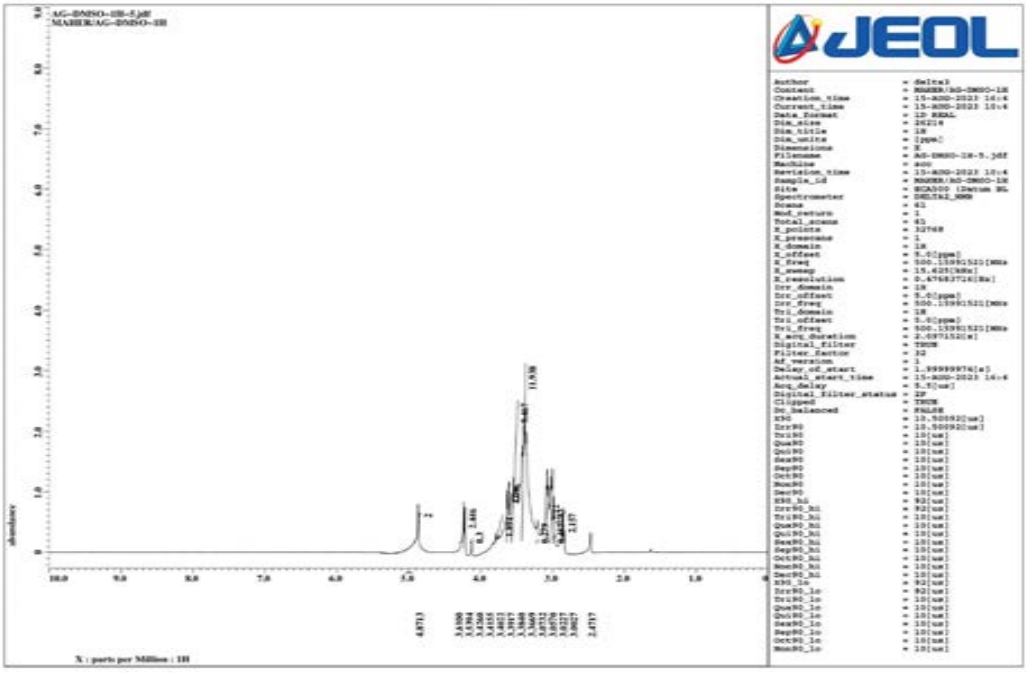

**Fig. 6.**

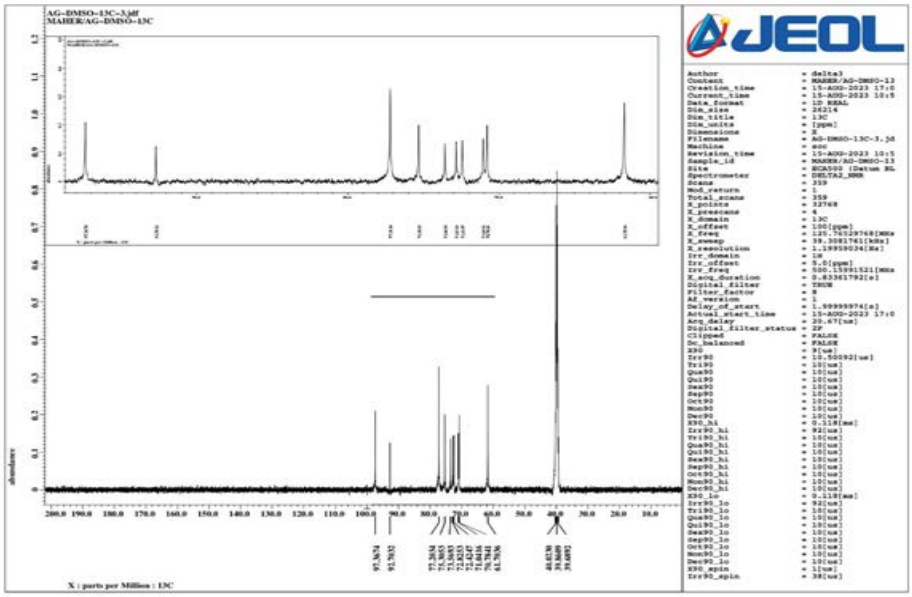


**Fig. 7.**

**Fig. 5-7.** The NMR analysis of the synthesized compound showed the presence of C12H22O11. Given the absence of aldehyde or ketone groups, the resulting compound can be identified as 1-2-O β D Glucopyranosyl α D glucose. The presence of C12H22O11 confirms the formation of the desired compound

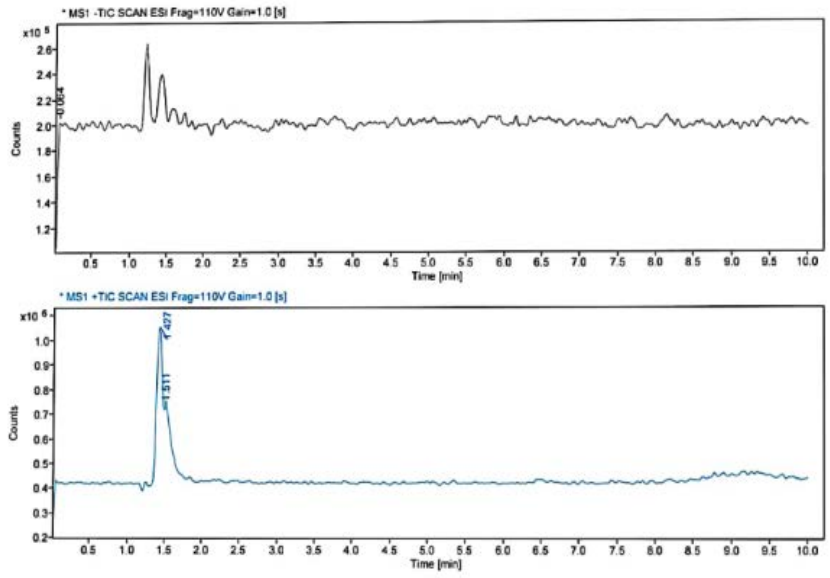


**Fig. 8.**

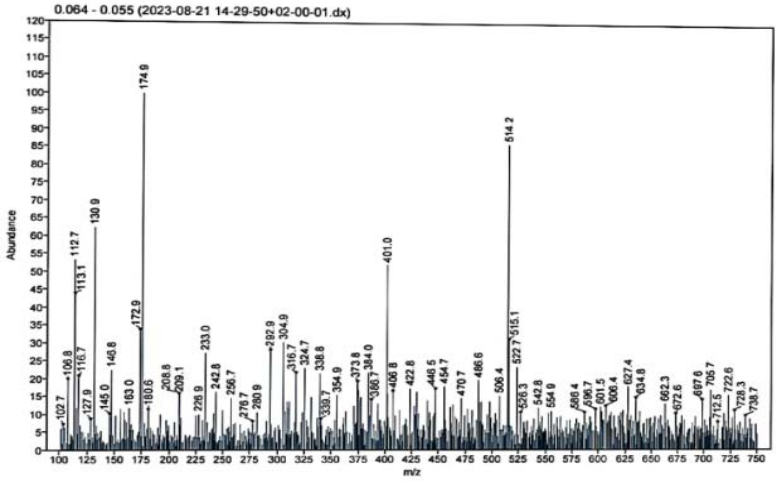


**Fig. 9.**

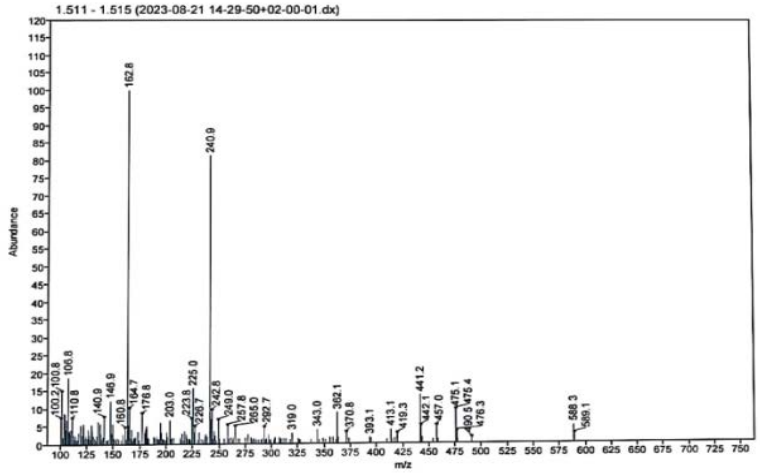


**Fig. 10.**

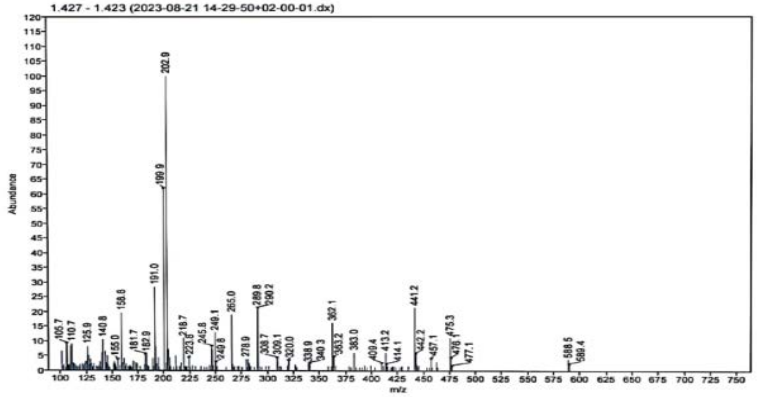


**Fig. 11.**

**Fig. 8-11.** The molecular mass of the monomer was determined to be 178.9 based on the results obtained from LC-MS analysis. Interestingly, the monomer shares a similar structural arrangement to trehalose, but it undergoes self-association to form the polymer through 1-2 linkages, resembling the molecular structure of sophorose

## THE SAFETY OF GLUCOSODIENE ON AN IN-VITRO BIOPSY CELL LINE MODEL

The laboratory experiment was conducted to evaluate the safety of Glucosodiene using an in-vitro biopsy cell line model. The BJ1 normal skin fibroblast cells were utilized for this study [19] (Table 1). First, the cells were suspended in DMEM-F12 medium supplemented with 1% antibiotic-antimycotic mixture and 1% L-glutamine. The cells were then batch cultured for 10 days. Afterward, the cells were seeded at a concentration of $10x10^3$ cells/well in 96-well microtiter plastic plates and incubated for 24 hours at 37°C under 5% $CO_2$. To assess cell viability, the mitochondrial-dependent reduction of yellow MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) to purple formazan was measured. The following steps were carried out in a sterile environment using a Laminar flow cabinet biosafety class II level. The cells were incubated either alone (negative control) or with different concentrations of Glucosodiene samples to achieve final concentrations of 100, 50, 25, 12.5, 6.25, 3.125, 0.78, and 1.56 ug/ml. After 48 hours of incubation, the medium was aspirated, and MTT salt (2.5µg/ml) was added to each well. The plates were further incubated for four hours at 37°C under 5% $CO_2$. To stop the reaction and dissolve the formed crystals, 10% Sodium Do-decyl Sulphate (SDS) in deionized water was added to each well and incubated overnight at 37°C. The absorbance was measured at 595 nm using a microplate multi-well reader with a reference wavelength of 620nm.

The percentage of change in viability was calculated using the formula: ((Reading of extract / Reading of negative control) -1) x 100). A profit analysis was conducted using SPSS 11 program to determine IC50 and IC90 values. The results of the experiment demonstrated that Glucosodiene exhibited no cellular toxicity or adverse effects on the BJ1 normal skin fibroblast cells at a concentration of 100 ppm (Figure 12, 13). This suggests the safety of Glucosodiene on normal cells in the in-vitro model [20, 21, 22].

**Tab. 1.** Summary

| Sample Code | $LC_{50}$ (µg/ml) | $LC_{90}$ (µg/ml) | Remarks |
|---|---|---|---|
| **glucosodiene molecules** | -------- | -------- | 0.3% at 100ppm |
| **DMSO** | -------- | -------- | 1% at 100ppm |
| **Negative control** | -------- | -------- | 0% |

Figure 12

A Control

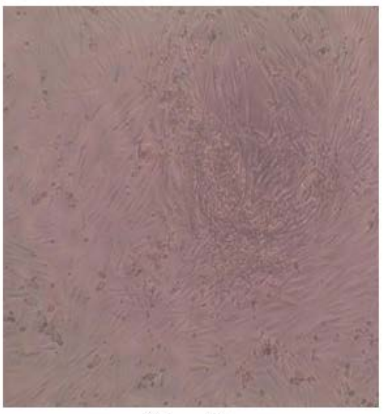

Figure 13

B Glucosodiene

**Fig. 12, 13.** The results of the experiment demonstrated that Glucosodiene exhibited no cellular toxicity or adverse effects on the BJ1 normal skin fibroblast cells at a concentration of 100 ppm

## POTENTIAL MECHANISMS OF ACTION OF GLUCOSODIENE POLYMER IN CANCER

Glucosodiene Polymer 1-2-O-β-D-Glucopyranosyl-α-D-glucose, a compound known for its significant anticancer properties, holds promise for cancer treatment. However, the precise mechanisms underlying its action remain unclear. In this study, we aim to explore the potential mechanisms through which Glucosodiene Polymer exerts its anticancer effects. Interestingly, the expected mechanism of action of Glucosodiene Polymer bears resemblance to the mode of action of compound 2-deoxy-D-glucose (2-DG). Glucose metabolism plays a crucial role in the rapid growth and proliferation of cancer cells. Glucosodiene Polymer disrupts this metabolic pathway, inhibiting the enhanced glucose metabolism

observed in cancer cells. By impairing energy production and essential biological processes required for cancer cell survival, Glucosodiene Polymer reduces cellular ATP levels, impacting diverse cellular functions and ultimately impeding tumor growth. More-over, Glucosodiene Polymer is anticipated to modulate signaling pathways involved in cancer cell survival and proliferation. Nota-bly, it may inhibit the activation of key protein kinases such as Akt and ERK, which are vital for cancer cell growth and survival. This interference with signaling pathways can induce cell cycle arrest and stimulate apoptosis, programmed cell death, in cancer cells. Furthermore, Glucosodiene Polymer may exhibit immune-en-hancing effects that promote an immune response against cancer. This can be attributed to its ability to induce cytokine production and activate immune cells, including stem cells and effector cells. These immune-modulatory properties of Glucosodiene Polymer contribute to its potential therapeutic efficacy in targeting tumors. It is important to note that, similar to compound 2-deoxy-D-glucose, lucosodiene polymer is expected to possess a favorable safety profile. Previous studies have indicated that 2-DG is well-tolerated and has minimal toxicity in normal cells. This suggests that Glucosodiene Polymer may also exhibit a similar safety pro-file, making it a promising candidate for cancer therapy. Further investigations are necessary to fully elucidate the mechanisms of action of Glucosodiene Polymer and its impact on tumor growth through its metabolic activity. These studies will provide valuable insights into the compound's efficacy, safety, and potential clini-cal applications in cancer treatment. Through its immune activity, Glucosodiene Polymer is likely to contribute to tumor suppres-sion and enhance anti-tumor immune response [23].

## A NOVEL TECHNIQUE FOR INDIVIDUALIZED TREATMENT OF CANCER DURING

### Diagnostic Biopsy to Determine Its Potential for Treatment with Glucosodiene

This hypothesis introduces a novel technique aimed at evaluating the potential therapeutic efficacy of Glucosodiene, an alkaline glu-cose isomer, for the treatment of cancer. The technique involves obtaining a diagnostic biopsy sample from the patient and sub-sequently performing an ex vivo tissue culture. The overall objec-tive is to assess the response of the patient's tumor tissue to Glu-cosodiene in order to establish a personalized treatment plan. The methodology of this technique involves several key steps. Firstly, a diagnostic biopsy sample is obtained from the patient using stan-dard procedures during the diagnostic phase to ensure accurate representation of the tumor tissue.

Secondly, the biopsy sample is transferred to the laboratory and placed in a suitable culture medium that closely mimics the physi-ological environment to maintain its viability. Subsequently, the biopsy sample is subjected to treatment with Glucosodiene. This can be achieved by directly adding Glucosodiene to the culture medium or administering it through a specific delivery system. Various concentrations and durations of exposure are tested to de-termine the optimal treatment conditions. The next step involves assessing the response of the tumor tissue to Glucosodiene. This assessment is performed through a range of analyses, including cellular viability assays, histological examination, gene expression profiling, and functional assays. These evaluations aim to deter-mine the impact of Glucosodiene on crucial cellular processes such as tumor growth, proliferation, and apotheosis. Following the assessment of tumor response, the data obtained from the ex vivo tissue culture experiments are subjected to rigorous analysis. This analysis aims to determine the efficacy of Glucosodiene in the specific patient's tumor tissue. Based on the observed response, a personalized treatment plan can be established, taking into con-sideration factors such as optimal dosage, treatment duration, and the potential for combination therapies. The utilization of ex vivo tissue culture during the diagnostic biopsy stage offers a valuable opportunity to evaluate the potential of Glucosodiene as a tar-geted therapy for breast cancer. By directly testing the patient's tu-mor tissue ex vivo, this approach enables individualized treatment decisions and holds the potential to enhance clinical outcomes. However, further investigations and thorough data analysis are necessary to validate the efficacy and safety of Glucosodiene as a personalized treatment option for cancer patients [24].

## SUCCESSFUL FIRST CASE TREATMENT FOR META-STATIC TRIPLE NEGATIVE BREAST CANCER (TNBC) OF BONE BY GLUCOSODIENE

This study investigates the use of glucosodiene as a potential treatment for metastatic Triple Negative Breast Cancer (TNBC) in the bones. Breast cancer is the most common type of cancer among women, and TNBC is a particularly aggressive subtype, accounting for 15%-20% of cases. TNBC lacks estrogen, proges-terone, and HER2 receptors, making it challenging to treat. The study focuses on the metabolic pathways in TNBC, particularly the Warburg effect, which is the reliance of cancer cells on glu-cose as their primary source of energy. Glucosodiene, an alkaline glucose isomer, is proposed as a therapeutic approach to inhibit glucose metabolism in tumors. It is believed that this inhibition can modify the tumor microenvironment and activate p53, a tu-mor suppressor protein. The case report presents a 43-year-old female patient with metastatic TNBC in the bones. The patient had previously undergone unsuccessful traditional chemotherapy. Treatment with glucosodiene for 15 days resulted in normal vi-tal functions and no signs of cellular activity. This suggests the potential effectiveness of glucosodiene as a targeted therapy for TNBC. The study aims to evaluate the use of glucosodiene as an individualized treatment for TNBC patients and establish effec-tive follow-up protocols. Ongoing research in this field focuses on developing new targeted therapies for TNBC, capitalizing on the altered metabolic pathways in cancer cells. This study explores the use of glucosodiene as a potential therapy for metastatic TNBC in the bones. The results indicate positive outcomes in terms of vital functions and cellular activity. Further research is needed to validate these findings and develop targeted therapies for TNBC patients. The case report features a 42-year-old female patient with TNBC who had previously undergone unsuccessful traditional chemotherapy and presented with bone metastasis. Following 15 days of glucosodiene treatment (Figure 14, 15), the patient exhibited normal vital functions and no signs of cellular activity [25].

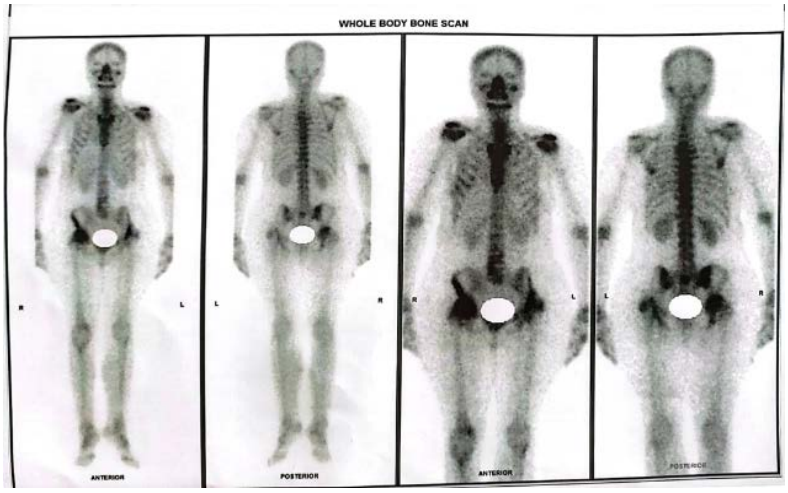


**Fig. 14.** This is the scan image of the patient prior to treatment or the latest bone scan before the decision to treat with glucosodiene. The patient presented with right leg pain, which prompted a bone scan revealing osseous metastasis in multiple locations, including the right iliac bone, head and trochanteric area of the right femur, right ischium, left acetabulum, and trochanteric area of the left femur. The publication of this image has been approved by the patient and the owner of this clinical study

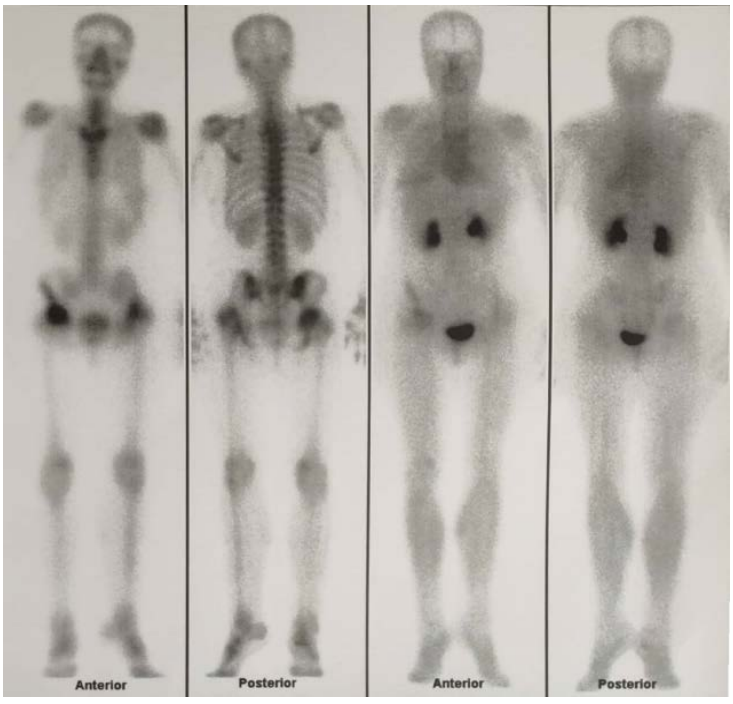


**Fig. 15.** This is an atomic scan image of the patient after treatment or with glucosodiene. An isotopic bone scan using dual-phase bone scintigraphy revealed consistent uptake of the tracer in the previously identified regions, accompanied by slight hyperemic changes during the blood pool phase. The remaining skeletal areas exhibited uniform distribution of the tracer, without any active or cold focal lesions. The publication of this image has been approved by the patient and the owner of this clinical study

## FOLLOW-UP INSIGHTS ON SUCCESSFUL FIRST CASE TREATMENT FOR METASTATIC TRIPLE NEGATIVE BREAST CANCER (TNBC) OF BONE AFTER A FOUR MONTH TREATMENT DURATION

### Imaging results

An F-18 Fluorodeoxyglucose (FDG) PET/CT scan was performed on a patient with a history of right breast cancer. The procedure involved administering F-18 FDG intravenously and imaging the patient approximately 60 minutes later using an integrated PET/CT scanner. A low-dose non-contrast CT scan was

conducted for attenuation correction and anatomical localization, followed by PET imaging from the skull vertex to the thighs. Additionally, a diagnostic post-contrast CT examination of the same regions was performed after intravenous administration of non-ionic contrast. The PET/CT images were reviewed in Tran's axial, coronal, and sagittal planes. The Standardized Uptake Value, maximum variant (SUV max), was calculated within regions of interest as necessary. The F-18 FDG PET/CT scan revealed metabolically active bilateral axillary, pectoral, and mediastinal lymph nodes, as well as metabolically active right external iliac and inguinal lymph nodes. Additionally, the scan suggested an old neglected case of right femoral Avascular Necrosis (AVN) with arthritic changes and left hip dislocation with pseudo arthrosis and arthritic changes. However, no hypermetabolic lesions were identified to explain loco-regional tumoral residue/recurrence, and no significant hypermetabolic lesions were detected in the remaining scanned areas of the body (Figure 16).

**Fig. 16.** An F-18 FDG PET/CT scan on a right breast cancer patient revealed metabolically active lymph nodes, including axillary, pectoral, mediastinal, external iliac, and inguinal nodes. The scan also suggested an old case of right femoral avascular necrosis and left hip dislocation. No hypermetabolic lesions indicating tumoral residue/recurrence were found, and the rest of the body showed no significant abnormalities in the PET/CT images

## Laboratory findings

### Biochemistry report:

The results of the liver function tests indicate that the levels of SGPT (Alanine Aminotransferase), SGOT (Aspartate Aminotransferase), ALP (Alkaline Phosphatase), GGT (G-Glutamyl Transpeptidase), total bilirubin, and direct bilirubin are within normal ranges.

The SGPT level is 19 U/L (reference range: up to 45 U/L), the SGOT level is 18 U/L (reference range: up to 40 U/L), the ALP level is 77 U/L (reference range: 40-100 U/L), the GGT level is 22 U/L (reference range: up to 45 U/L), the total bilirubin level is 0.7 mg/dL (reference range: up to 1.2 mg/dL), and the direct bilirubin level is 0.22 mg/dL (reference range: up to 0.25 mg/dL). The kidney function tests reveal normal levels of serum creatinine and blood urea. The serum creatinine level is 0.9 mg/dL (reference range: 0.6 mg/dL-1.4 mg/dL), and the blood urea level is 24 mg/dL (ref-erence range: 15-45 mg/dL).

## Hematology report

The hematological parameters show normal values. Th e h emoglobin (Hgb) level is 13.9 g/dL (reference range: 11.7 g/dL -15.5 g/dL), the Red Blood Cell count (RBCs) is 4.4 x $100^3$ Cells/µL (reference range: 3.8-5.1 x $100^3$ Cells/µL), the Hematocrit (Hct) is 41.6 % (reference range: 35% - 45%), the platelet count (Plt) is 186 x $10^3/mm^3$ (reference range: 150-440 x $10^3/mm^3$), and the White Blood Cell count (WBCs) is 8.4 x $10^3/mm^3$ (reference range: 4.5 - 11.0 x $10^3/mm^3$).

These laboratory findings provide valuable information regarding the liver and kidney functions, as well as the hematological parameters. The liver function tests indicate that the patient's liver is functioning within normal limits, with no signs of liver damage or impaired function. The kidney function tests suggest that the kidneys are functioning properly, with no evidence of impaired renal filtration or excretion. The hematological parameters reveal that the patient's blood components, including red blood cells, white blood cells, and platelets, are within the normal range.

### Impression of case:

The presented case study revolves around a 43-year-old female patient diagnosed with metastatic Triple Negative Breast Cancer (TNBC). The patient's initial presentation included a palpable mass, pain, fatigue, and weight loss in the right breast. Despite traditional chemotherapy proving unsuccessful, treatment with glucosodiene, an alkaline glucose isomer, resulted in the restoration of normal vital functions and the absence of cellular activity. The follow-up evaluation comprises comprehensive medical imaging and laboratory findings. The F-18 Fluorodeoxyglucose (FDG) PET/CT scan revealed metabolically active lymph nodes but lacked hypermetabolic lesions indicative of loco-regional tumoral residue/recurrence. Liver and kidney function tests, along with hematological parameters, exhibited values well within normal ranges. Notably, the liver function tests showed no signs of damage or impaired function, the kidney function tests suggested proper renal filtration, and the hematological parameters indicated normal blood components.

In light of these results, there is no medical indication suggesting the recurrence of breast and bones cancer metastasis after treat-

ment. The comprehensive evaluation of imaging and laboratory findings provides assurance regarding the patient's general health status and underscores the efficacy of glucosodiene. The absence of hypermetabolic lesions in vital areas, coupled with normal liver and kidney functions, reinforces the conclusion that the patient is not exhibiting signs of recurrent renal cancer. This robust evidence supports the notion that glucosodiene has been effective in the individualized treatment of TNBC, paving the way for further research and the establishment of follow-up protocols in similar cases.

## MEDICAL GUIDANCE AND INTEGRATED THERAPEUTIC APPROACH: THE PROTOCOL OF GLUCOSE

### Mutation Theory via Glucosodiene and indication of Positive Tumor Lysis Syndrome

Glucosodiene, an alkaloid isomer of glucose, is employed in the treatment of cancerous tumors characterized by their aggregation. Its potential mechanism involves inhibiting the Warburg effect, thus preventing its impact within the tumor. The mechanism in-cludes modifying the tumor's acidity, reactivating programmed cell death enzymes, and promoting tumor disintegration, known as Tumor Lysis Syndrome (TLS). This life-threatening condi-tion occurs in patients of all ages undergoing cancer treatment, involving the rapid release of cellular contents from cancer cells into the bloodstream due to their breakdown, either spontane-ously or as a result of cancer treatment. This release leads to sig-nificant abnormalities in electrolytes, including elevated levels of uric acid, potassium, and phosphate in the blood, along with decreased calcium. The severity of TLS increases with the degree of the underlying malignant tumor and its spread. Therefore, in-terventions targeting the tumor, such as glucosodiene identified in PT scans for treated patients with observed disappearance or disintegration of hotspots in their medical scans supporting this conclusion, may require specific medical guidance based on tumor location, stage, and patient health. TLS management poses signifi-cant challenges, with ongoing research focusing on optimal risk assessment and treatment strategies [26]. Several guidelines and recommendations have been developed to guide healthcare pro-fessionals in managing TLS. These emphasize risk stratification, early identification of high-risk patients, and preventive measures to impede TLS development. Preventive measures may include aggressive hydration, uric acid-lowering agents, and managing electrolyte imbalances with electrical conductance alternatives. In addition to preventive measures, prompt and appropriate TLS management is crucial [27]. This may involve meticulousmonitoring of electrolyte levels, correction through pharmacological interventions, and supportive care to address complications [28].

Specific drugs, such as allopurinol, losartan in cases of hyperten-sion and SGLT2 inhibitors in diabetic patients, can effectively control elevated blood uric acid [29]. Interventions to control electrolyte imbalances such as calcium gluconate administration for hypocalcemia or kidney dialysis for acute renal failure may be necessary in some cases [30-32]. The use of anti-inflammatory and relatively immune-safe analgesics, like celecoxib, is recommended due to their tumor-suppressing and anti-spreading properties [33, 34]. Therefore, laboratory monitoring plays a vital role in TLS management. Regular assessment of uric acid, potassium, phos-phate, calcium, and kidney function is essential for detecting and monitoring electrolyte imbalances and renal failure. The timing and frequency of laboratory tests may vary based on tumor size and clinical presentation. Close collaboration between oncologists, hematologists, and clinical laboratory specialists is crucial to ensure accurate and timely laboratory testing, interpretation, and intervention [35].

### The assessment and initial management of the Tumor Lysis Syndrome

According to the algorithm presented in (Figure 17), the assess-ment and initial management of the Tumor Lysis Syndrome are as follows:

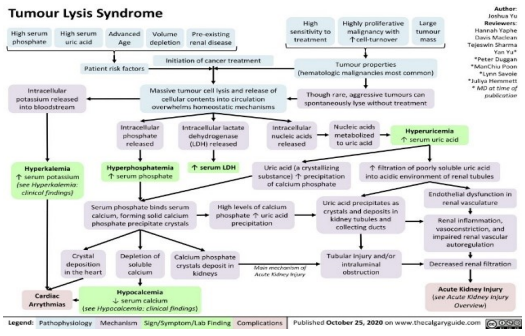


**Fig. 17.** The presented algorithm, depicted in Figure 17, delineates a systematic approach to the assessment and initial management of Tumor Lysis Syndrome (TLS) upon patient presentation. Subsequent care is contingent upon the patient's progression. Tumor lysis syndrome, at times, unpredictably manifests in patients deemed low risk, necessitating a more assertive treatment approach. Conversely, certain high-risk patients exhibit no signs of TLS following initial treatment days, thereby warranting less intensive care thereafter. The evaluation of risk factors associated with TLS mandates clinical acumen. Determining whether mild or transient dehydration, the size of a cancer mass, or the potential for cell lysis is of medium or high risk can be challenging. In ambiguous scenarios, additional criteria serve to elucidate the risk level. An elevated lactate dehydrogenase level (>2 times the upper limit of the normal range) and an elevated uric acid level at presentation are indicative of an augmented TLS risk. These parameters aid in categorizing borderline cases into appropriate risk groups. In instances where differentiation between two risk categories proves challenging, a prudent approach advocates treating the patient as if belonging to the higher-risk category. Notably, the algorithm is crafted for utilization by both oncologists and non-oncologists, adopting a conservative methodology to enhance safety. The term "bulky tumor" encompasses the tumor mass originating from metastatic lesions, with TLS denoting Tumor Lysis Syndrome

### Patient presentation:
The algorithm provides a guide to care when the patient presents with symptoms of tumor lysis syndrome.

### Subsequent care:
The subsequent care depends on how the patient progresses. Some low-risk patients may unexpectedly develop tumor lysis syndrome and require more aggressive treatment. On the other hand, some high-risk patients may not show evidence of tumor lysis syndrome after a few days of treatment and may need less intensive care.

### Assessment of risk factors:
Assessing risk factors for tumor lysis syndrome requires clinical judgment. It may be unclear whether mild or transient dehydration should be considered, the size of a cancer mass (medium or large), or the potential for cell lysis with a specific treatment (medium or high). In such cases, other criteria can be helpful. An elevated lactate dehydrogenase level (>2 times the upper limit of the normal range) and an elevated uric acid level at presentation are associated with an increased risk of tumor lysis syndrome. These criteria can be used to classify borderline cases into an appropriate risk group.

### Treating borderline cases:
If it is difficult to distinguish between two risk categories, it is recommended to treat the patient as if he or she is in the higher-risk category. This approach ensures appropriate management and minimizes the risk of complications.

### Conservative approach:
The algorithm is designed for use by both oncologists and non-oncologists, and it emphasizes a conservative approach to maximize patient safety [36].

## Comprehensive laboratory monitoring in tumor lysis syndrome: assessing severity, treatment response, and complications

During the presence of tumor lysis syndrome, certain medical laboratory tests are necessary to assess the patient's condition and monitor the associated metabolic abnormalities. These tests help in evaluating the severity and extent of tumor involvement as well as providing indicators of treatment response and potential complications. The following are the key laboratory tests recommended for patients with tumor lysis syndrome.

### Uric Acid:
Uric acid is the end product of purine metabolism and is often elevated in tumor lysis syndrome. Measuring uric acid levels helps in assessing the extent of tumor lysis and the risk of uric acid nephropathy. Elevated levels indicate increased tumor burden and may necessitate uric acid-lowering interventions.

### Potassium:
Hyperkalemia is a common electrolyte abnormality in tumor lysis syndrome. Monitoring potassium levels is crucial to detect and manage any potential cardiac arrhythmias or other complications associated with hyperkalemia.

### Phosphorus:
Tumor lysis can lead to the release of intracellular phosphate, causing hyperphosphatemia. Elevated phosphorus levels can result in hypocalcemia and subsequent complications such as tetany and cardiac dysrhythmias. Regular monitoring of phosphorus levels helps guide appropriate interventions.

### Calcium:
Hypocalcemia can occur due to the deposition of calcium phosphate crystals in various organs as a consequence of elevated phosphorus levels. Monitoring calcium levels is important to detect and manage related symptoms such as neuromuscular irritability and dysrhythmias.

### Creatinine:
Creatinine is a marker of renal function and is commonly elevated in tumor lysis syndrome due to acute kidney injury. Serial measurements of creatinine levels help assess the degree of renal impairment and guide appropriate management, including the need for renal replacement therapy.

### Complete Blood Count (CBC):
A CBC with differential is essential for evaluating the patient's hematologic profile. It helps identify abnormalities such as leukocytosis, leukopenia, anemia, or thrombocytopenia associated with the underlying malignancy and its treatment.

### Lactate Dehydrogenase (LDH):
LDH is an enzyme found in various tissues, including tumor cells. Elevated LDH levels are often observed in tumor lysis syndrome and can serve as a marker of disease burden and response to therapy.

### Alkaline Phosphatase (AIP):
Aryl Hydrocarbon Receptor-Interacting Protein, stands out as a pivotal biomarker in assessing tumor regression in hematologic malignancies. Its modulation of the Aryl Hydrocarbon Receptor (AhR) pathway reflects dynamic cellular responses to stressors induced by cancer. Monitoring AIP levels not only gauges treatment efficacy but also holds prognostic value, aiding in predicting sustained regression and potential relapse [37]. AIP's multifaceted role opens avenues for targeted therapeutic research, enhancing our understanding of cancer biology and refining treatment strategies. It is important to note that the specific tests ordered and their frequency may vary depending on the individual patient's clinical presentation and the treating physician's discretion. Regular monitoring of these laboratory parameters allows for early detection of metabolic derangements, guiding appropriate interventions, and optimizing patient outcomes [38].

## Clinical Indicators and Observations Protocol for Patients Undergoing Tumor Lysis Syndrome Treatment with Glucosodiene

The treatment protocol, spanning an average of twenty days, is categorized into four stages, each lasting five days. Following a minimum 24-hour carbohydrate and sugar restriction before treatment initiation, involving a daily oral dose of 100 ml of glucosodiene, administered Daily.

- Stage One (Day 1-5); Patients experience improved

sleep quality, and tumor dissolution transitions from a firm to a slightly relaxed texture. Stage Two (Day 6-10); Significant improvements are observed, with enhanced vital organ functions, reduced pain sensation, and lower doses of analgesics for patients in advanced neoplastic stages. Clinical indicators correlate with tumor lysis analysis milestones.

- Stage Three (Day 11-15); Patients begin to notice neurological improvements, particularly in areas affected by prior treatments like chemotherapy, demonstrating increased environmental responsiveness.
- Stage Four (Day 16-20); Vital signs and clinical indicators approach near-normal values. Subsequently, patients undergo a PT scan for pre-and post-treatment tumor spread and dissolution comparison. It is crucial to emphasize the significance of carbohydrate and sugar restriction, ensuring optimal Glucosodiene absorption and compelling the body to adapt to it as a primary nutritional source. This dietary adjustment plays a vital role in treatment efficacy, enhancing the overall therapeutic outcomes.

## DISCUSSION

Cancer cells exhibit an increase in glucose uptake through the up regulation of glucose transporters, which fuels their rapid growth and proliferation. Maybe Glucosodiene works by inhibiting glucose metabolism within tumors, impairing energy production, and altering the tumor's microenvironment acidity. This disruption impedes tumor growth and spread, potentially leading to cell death. Maybe Glucosodiene also regulates signaling pathways involved in the survival and spread of cancer cells, inhibiting crucial protein kinases and promoting cell cycle arrest and programmed cell death. Additionally, it may enhance the anti-tumor immune response by stimulating cytokine production and activating immune cells. The successful treatment of Triple Negative Breast Cancer (TNBC) in bones using glucosodiene highlights its potential as an effective therapy for advanced-stage cancer. A case report demonstrates the ability of glucosodiene to inhibit cellular activity and underscores its clinical significance in targeting cancer metabolism. Research studies proposing and discussing the impact of glucosodiene as a promising theory for cancer treatment have shed light on its ability to modify glucose and endow it with alkaline properties.

This modification potentially allows for the destruction or metabolic inhibition of glucose within the tumor, a phenomenon known as the Warburg effect. This approach and its results may herald a new branch of chemotherapy known as "toxinutromedicanical-chemotherapy" [40].

This field can be defined as a science dedicated to exploring the possibility of modifying cellular nutrition, specifically glucose "Glucose Mutation", and imbuing it with chemical, alkaline, and therapeutic properties through substitution reactions or by loading therapeutic agents onto glucose. Based on the glucolipotoxicity theory, an innovative approach deserving investigation for cancer-prone individuals and those with a medical history involves the use of Glucagon-Like Peptide-1 (GLP-1) agonists as a preventive measure against cancer. The glucolipotoxicity theory posits that the accumulation of glycolipids within cells plays a crucial role in cancer development. In this context, GLP-1 agonists emerge as potential protective agents, targeting the disruptions in cellular homeostasis associated with glycolipid accumulation. GLP-1 agonists, known for their regulatory effects on glucose and lipid metabolism, may counteract the glycolipid-induced closure of glucose transporters on cancer cell membranes. This preventive strategy aligns with the broader understanding provided by the glucolipotoxicity theory, suggesting a promising avenue for further investigation into the role of GLP-1 agonists in mitigating cancer risk for susceptible individuals, particularly those with a medical history indicative of heightened susceptibility to cancer [39]. Consequently, this approach achieves direct killing of cancer cells through their metabolic activity and their avidity for glucose. The promising results demonstrated by glucosodiene merit further investigation and study within this emerging field.

According to the established therapeutic protocol documented in the case of a patient who attained remission from triple-negative breast cancer, and subsequent to comprehensive safety evaluations within the physiological context, glucosodiene is synthesized via a chemical reaction involving 3.5 grams of dextrose and 2.5 grams of sodium bicarbonate in a meticulously filtered aqueous solution measuring 100 milliliters. This synthesis process entails controlled heating for approximately 120 seconds, a duration calibrated to coincide with the appearance of gas bubbles, indicative of carbon dioxide release. The therapeutic dose of glucosodiene, administered orally once daily at intervals of 24 hours in a volumetric dose of 100 milliliters, has been established as the recommended standard. It is elucidated that within each 100 milliliters of the glucosodiene solution, a dosage equivalent to 85.71 milligrams of glucosodiene per kilogram of body weight is inherently encapsulated.

## CONCLUSION

Glucosodiene, also known as the "glucose mutation" holds great promise as a therapeutic strategy for cancer treatment. It exhibits inhibitory effects on glucose metabolism, modulates signaling pathways, and possesses immune-enhancing properties, making it an attractive candidate in the fight against cancer.

However, further research is necessary to fully comprehend the underlying mechanisms of action and optimize the therapeutic potential of glucosodiene. With ongoing investigations, glucosodiene has the potential to revolutionize cancer treatment by exploiting the metabolic vulnerabilities of cancer cells and offering personalized and effective treatment options.

## LIMITATIONS OF THE STUDY

In the early stages of conceptualizing the Maher Akl Theory, commonly known as the Glucose Mutation, the primary objective was not merely the formulation or advancement of the theory itself. Instead, the focus was on the preliminary support of the theory, even if with a limited number of experimental subjects – only four mice. The aim was to establish a foundational backing for the theory. However, it is crucial to acknowledge that this approach led to less precise results, as highlighted in previous publications. Initial assumptions centered on the belief that alkaline elements would

dissolve tumors. With the emergence of the first healing case, it became apparent that the compound Glucosodiene inhibits glucose oxidation within the tumor, resembling the mechanism of the compound 2-deoxy-D-glucose. Additionally, its alkaline properties contribute to restoring the tumor's alkaline hydrogenic environment. These insights underscore the evolving understanding of Glucosodiene's role and emphasize the necessity for cautious interpretation given the initial conceptual framework [13].

These experiments were conducted in vivo, deviating from the cell line experiments previously performed on ETM6 cells. Furthermore, safety tests specific to the compound glucosodiene Tested. The documentation of these effects is presented in this manuscript, including NMR and LC-MS tests, aiming to authenticate the glucosodiene polymer. These experiments were conducted based on the available resources and capabilities, as the manuscript and theory have not received any support. Therefore, further experiments and research are needed to substantiate the validity of the theory and the compound. Additionally, all the clinical observations resulting from the accidental administration of glucosodiene solution, as documented in the case report of a woman with metastatic triple-negative breast cancer to the bones, were analyzed in this manuscript. The results were built upon the case's confirmation, clinical examinations, and the findings, suggesting that the glucosodiene polymer may function through a mechanism similar to that of 2-deoxy-d-glucose compounds. Regarding the mechanism of action of this compound in cancer treatment, acting as a d-glucose mimic, 2-deoxy-d-glucose (2-DG) inhibits glycolysis by forming and accumulating 2-deoxy-d-glucose-6-phosphate (2-DG6P) intracellularly. This inhibition affects the function of hexokinase and glucose-6-phosphate isomerase, ultimately inducing cell death. Moreover, considering that glucosodiene compounds have alkaline effects, clinical observations suggest a potential correlation with the prevention and inhibition of cancer metastasis. Therefore, the limited support received for this hypothesis necessitates extensive attention from researchers and scientists to address any gaps in the chemical description of the compound, preclinical and post clinical experiments, and further exploration.

### STATEMENT OF ETHICAL APPROVAL OR INFORMED CONSENT FOR CASE STUDIES

In conducting this case study, adherence to the principles outlined in the Declaration of Helsinki was ensured. The study also met the criteria for care guidelines, and informed consent was obtained from the patient for follow-up, including permission for the publication of all photographs, laboratory findings, and images presented in this report. The trial registration details for this case study are as follows: NCT05957939.

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## STATEMENTS AND DECLARATIONS

The authors declare that there are no conflicts of interest.

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