

The Detailed Description Mechanisms of the Herbs Extracts Operations in the New Method Cancer Disease Treatment via the Rearrangement of Metabolism from Pathological Development into Normal Development

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Abstract

The article displays continuation of the accepted for publication in "Journal of Clinical Trials" article entitled "The new method cancer disease treatment making the rearrangement of metabolism from pathological development into normal development". There were described the positive results of cancer treatment by the new method of cancer disease treatment which was borrowed from the folk healers. These results were achieved by treatment of sick patient Ch. with "Metastatic cancer the intermediate bronchus of the right lung the IY degree, clinical stage IY". Taking into account the great experience of folk healer Breuss in treatment of various cancer diseases, Breuss recommendations concerning use of the herbs extracts were appreciated, representing mechanism operating of the tendered extracts of herbs in condition "Prolonged Medical Starvation" of the new method treatment of cancer disease. The roles of the tendered extracts of herbs in bringing cancer metabolism to depression was analyzed considering the shift of the metabolism both in an organism and in cancer tissue due to condition of Prolonged Starvation. Also it was appraised the possible using light cytotoxic agents in very small dosage with the condition "Prolonged Medical Starvation" of the new method cancer treatment for the full cure of patient. The negative influences of big dosage cytotoxic anti-cancer drugs on an organism were elucidated estimating the use of light cytotoxic agents in very small dosage in the condition "Prolonged Medical Starvation" of the new method cancer treatment. Also the possible mechanisms of drug resistance were explained referring outcomes of experiments some authors. Besides the advantage of the offered new method cancer treatment was estimated considering the mechanism operation of this method and the mechanisms of drug resistance by chemotherapeutic treatment in up-to-date methods cancer disease treatment. Thus it was supposed the possible modes to integrate the offered new method treatment of cancer disease with the modern methods treatment of cancer disease considering the role of the extracts of herbs for cancer treatment in condition of Prolonged Starvation. However the integration of the offered new method treatment of cancer disease with the modern methods treatment of cancer disease should be made after detailed clinical trials.

Keywords: Warburg effect; Cancer therapy; Cytostatic effect; DNA or RNA inhibition; Tyrosine kinases; Glycolysis inhibition; Cytotoxic drugs; Cytostatic drugs

Introduction

The new method treatment of cancer disease was borrowed from the folk healers Breuss [1,2]. The author has cured the ill man at the stage of incurable cancer using "Medical Starvation during 45 days" and "Winter Bathing" (in an ice-hole) according to data of folk healers Breuss and maintenance an organism by extracts of herbs corresponding to recommendation of Breuss [1,2]. Austrian folk healer Breuss [1,2] described recommendations for use of the extracts of herbs which promote the positive results in oncologic diseases treatment using "Medical Starvation during 42 days". Breuss recommendations concerning the extracts of herbs were described in the article. The author gives the scientific explanation of the mechanisms extracts of herbs operation in condition of Prolonged Medical Starvation (Figure 1). Estimating mechanisms resistance to the cytostatic and cytotoxic effects of drugs, it was compared reparative mechanisms of normal cellular development and cellular damage caused by cytotoxic drugs and was offered possible concepts of some mechanisms promoting resistance to the cytostatic and cytotoxic effects of drugs. Having compared the new method treatment with the up-to-date methods treatment, it was described the advantage of the new method of cancer treatment. The peculiarity of the metabolism of a human organism is that the entering of substances into an organism takes place from Environment with food. A malignant tumor being inside the organism uses an organism as Environment, and entering of substances into tumor takes place from depots of an organism (fatty and other depots) (Figure 2). Therefore the long starvation of an organism creates the condition of competition between an organism and a tumor for the

use of depots as the source of substances for metabolism. Therefore Prolonged Medical Starvation leads to cancer depression and the light cytotoxic remedy (or cytostatic remedy) ruins the metabolism of cancer disease that was reflected in mechanisms operations of the new method cancer treatment using tendered extracts of herbs. All these data gave an opportunity for the author's supposition of the possible integrative therapies between offered new method cancer disease treatment and some modern methods treatment which should be made after detailed Clinical Trials.

Construction and contents of the figures

The figure 1 shows:

- Oxidative catabolic exoergonic processes in the organism, reflecting also processes of excretion of oxidized substances (the arrow below the figure), are presented with brief biochemical scheme of transition from glycolysis to tricarboxylic acids Krebs cycle.

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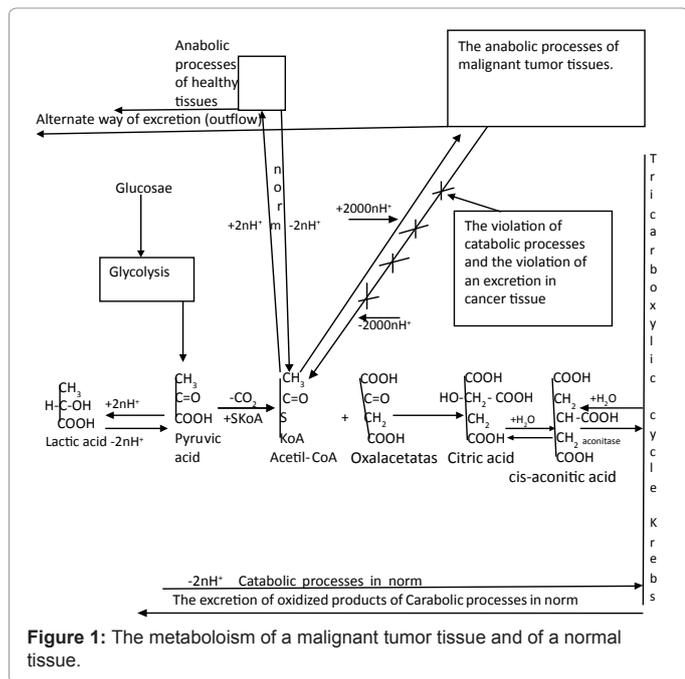


Figure 1: The metabolism of a malignant tumor tissue and of a normal tissue.

The directions of anabolic processes metabolism in the organism and malignant tumor are presented with arrows directed upward and downward from the nodal point of ramification of anabolic and catabolic processes at "Acetyl-CoA".

The anabolic endoergonic processes in an organism going on in normal quantity are presented with a short arrow directed upward and marked with reductive processes " $+2nH^+$ "/inflow protons, being defined in the anabolic processes as energy consumption (inflow).

The anabolic endoergonic processes in a malignant tumor going on in a huge quantity are presented with a long arrow directed upward and marked with huge quantity reductive processes " $+2000nH^+$ "/inflow protons, being defined in the anabolic processes as energy consumption (inflow).

Processes of oxidative catabolic excretion from an organism of high-molecular substances, been formed as the result of anabolic processes, are presented with a short arrow directed downward and marked with oxidation processes " $-2nH^+$ "/outflow protons, being defined in catabolic anaerobic processes as energy outflow.

The disable oxidative excretion of high-molecular substances, synthesized in anabolic processes of a malignant tumor, as the result of "overload of the nodal point of ramification of anabolic and catabolic processes" and "Acetyl-CoA deficit for oxidative processes" are presented with the crossed out long arrow directed downward and marked with oxidative processes " $-2000nH^+$ " the crossed out of outflow necessary for excretion protons, that are defined in catabolic anaerobic processes as disturbance energy outflow.

The alternative excretion of high-molecular substances in the structure of rejecting cells occurring in a small quantity in an organism is presented with a short arrow.

The alternative excretion of high-molecular substances in the structure of rejecting cells occurring in a huge quantity in a malignant tumor due to the blocking of the oxidative excretion of these substances is presented with a long arrow.

The figure 2 shows:

The inflow of Energy and Substances into an organism in section "The initial level of a metabolism" (gastrointestinal tract).

Catabolic processes of Metabolism via full aerobic oxidation with production of additional calories for maintenance of stable stationary state of an Internal Energy (U) an organism via temperature $36.5^{\circ}C-37.6^{\circ}C$ by which all enzymes operate in an organism and for maintenance of the stability of biochemical indices of substances concentrations in Interior Medium of blood and neurolymph of an organism in section "The Base level of a metabolism of Internal Medium".

Catabolic processes of Metabolism via the incomplete anaerobic oxidation with the additional energy production for an organism operation: The Useful Work (W_{use}) of internal vital organs of an organism operation (heart, brain, nervous system, liver and the other organs) and the External Work (W_{ext}) of a person (mechanical works of muscles, production of heat /calories/mental work and so on) in section "The Base level of a metabolism of Internal Medium" blood, neurolymph, liver etc.

Anabolic biosynthetic processes of Metabolism for tissue growth, biosyntheses of all chemical substances, hormones, enzymes, immune bodies and so on in section "The Biosynthetic level of a metabolism" in liver, in the cells of the Reticuloendothelial System (RES) and so on.

The outflow of Energy and Products of metabolized substances in section Environment: a) Carbon dioxide (CO_2) and endogenic water (H_2O_{end}) as products of full aerobic oxidation through lung, b) Products of the anaerobic incomplete oxidation through uropoiesis,

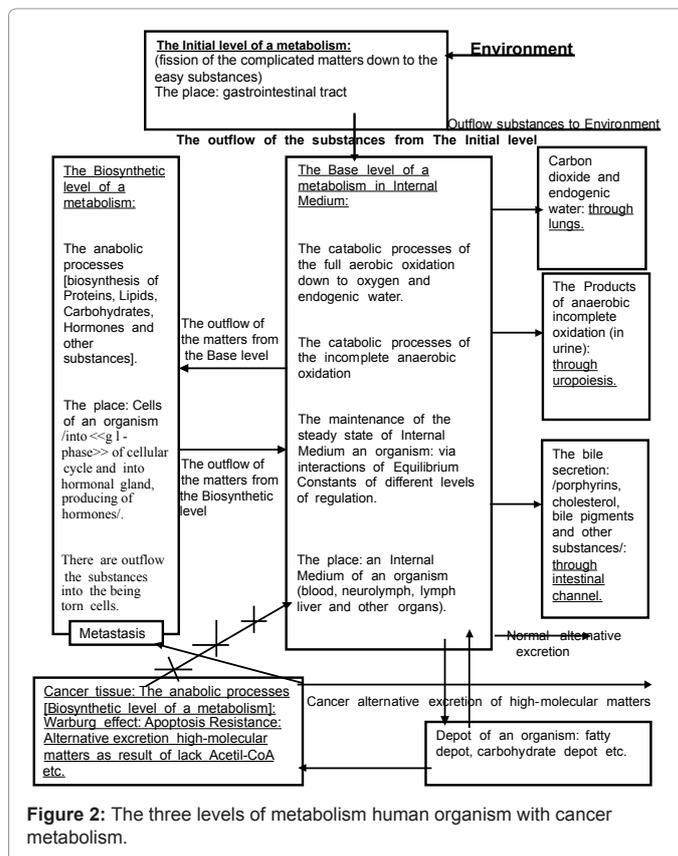


Figure 2: The three levels of metabolism human organism with cancer metabolism.

c) The bile secretion: porphyrins, cholesterol, bile pigments and the other substances through intestinal channel.

- Cancer tissue: The huge anabolic processes, Warburg effect in metabolism, Cancer alternative excretion of high-molecular substances.
- Metastasis of Cancer.
- Depot of an organism: fatty depot, carbohydrate depot etc.
- The reciprocal interactions between all of sections are represented by arrows, which are directed to both directions.

The detail description of the treatment by “Prolonged medical Starvation 42-45 days” following up the Breuss recommendations concerning use of herbs extracts in condition of “Prolonged medical Starvation” [1,2]. Taking into account the great experience of folk Breuss in treatment of various cancer diseases, Breuss recommendations concerning use the extracts of herbs were accepted. Here are Breuss recommendations concerning application of the herbs extracts [1,2].

The three teas for all types of cancers should be used: sage tea, kidney tea and cranesbill tea. Sage tea includes sage (*Salvia officinalis*), St. John’s wort (*Hypericum perforatum*), peppermint (*Mentha piperata*) and balm (*Melissa officinalis*). One teaspoon or maximum two teaspoons of sage should be poured into boiling water and boiled only three minutes. Then sage should be eliminated via filtering through a triple gauze layer in order that any fibre must not remain in the extract. St. John’s wort (*Hypericum perforatum*), peppermint (*Mentha piperata*) and balm (*Melissa officinalis*) should be poured into this hot extract, extracted ten minutes more and then filtered through a triple gauze layer. Thus sage tea is obtained as the extract of these herbs.

Kidney tea includes horsetail (*Equisetum arvense*)-15 grams, stinging nettle (*Urtica dioica*)-10 grams, knotgrass (*Polygonum aviculare*)-8 grams and St. John’s wort (*Hypericum perforatum*)-6 grams. The mixture pinches of these herbs should be put for ten minutes into a cup of hot water. Then these herbs mixture should be filtered through a triple gauze layer. The hard rest of herbs mixture must be poured with hot water and boiled ten minutes more. Then herbs mixture should be again filtered and both these filtered liquids should be mixed. The explanation of such mode of preparation kidney tea is that there are the required substances in the filtered liquid of these herbs mixture which should not be boiled due to destruction to these substances. However there is silicic acid in the hard rest of herbs mixture which can be received by ten minutes boiling. Breuss notes that kidney tea must be taken only for the first three weeks.

Cranesbill tea includes red cranesbill (*Geranium robertianum*). The pinch of the red cranesbill (*Geranium robertianum*) should be put for ten minutes into a cup of hot water and filtered through a triple gauze layer. Only one half cup of cold Cranesbill tea should be ingested per day. Breuss notes that red cranesbill (*Geranium robertianum*) contains the small quantity of radium. Thus the new method of treatment is integrated maybe with up-to-date methods of treatment partially via using the small quantity of radium as the cytotoxic remedy (or cytostatic remedy) in condition of the prolonged medical starvation.

Besides Breuss offers to use during treatment via starvation 42 days the Vegetable Juice Mixture which consists of 55% red beet root-300 grams, 20% carrots-100 grams, 20% celery root-100 grams, 3% raw potato-10 to 30 grams options, and 2% Black Radish-10 to 30 grams. He notes that the Vegetable Juice Mixture should not be drunk more than half a liter per a day. It should be mixed all these vegetables in a juicy and then be filtered to get free from any sediment. Before starting

the treatment it can try one quarter liter of this juice per day taking this juice by the spoonful. So Breuss notes that the potato is optional except for liver cancer where it plays an important role.

The Breuss instructions claim to take one half cup of cold kidney tea first thing in the morning for the purpose of habituation. Then 30 to 60 minutes later two cups warm herb tea made from St. John’s Wort, Peppermint and Lemon Balm should be taken. After another 30 to 60 minutes a little vegetable juice is taken, and it should be well salivated before swallowing. Fifteen to 30 minutes later another sip of vegetable juice is taken. It should be taken 10 to 15 times throughout the morning but only when patient feels like it. Then patient can drink warm or cold sage tea without sugar, as much as he like. At noon the patient can take one half cup of kidney tea and again before retiring at night. At the afternoon the patient must take a few sips of tea. Any liquid should be sipped and well salivated. Kidney tea should be taken only during the first three weeks of the treatment. Also R Breuss insists on urgent request to drink one cup of cold Cranesbill tea (*geranium robertianum*) per day throughout the time of therapy. Besides Breuss recommends for cancer treatment of the bones and lungs, prepare a tea of Plantain (*plantago major*), Icelandic Moss, Lungwort, ground Ivy and Mullein.

The mechanism operation of “Prolonged medical Starvation during 42-45 days”

Cancer tumor is located inside the human organism using the organism as Environment, and obtains the substances for its metabolism from depot of the organism (“Depot of an organism”) (Figure 2). However the organism obtains also substances for its metabolism from depot of the organism in condition of treatment by “Prolonged medical Starvation” (during 42-45 days) because of absence function inflow of substances from the Environment into an organism. Besides, the treatment by “Prolonged medical Starvation” (during 42-45 days) causes exhaustion almost of all depots (especially fat depots) of an organism. Therefore this method treatment leads to the competition between the cancer tissue and the organism for the use of remained exhausted depot to maintain via catabolic metabolism of the normal temperature (36.0°C–37.5°C) by which the all enzymes operate. The aerobic catabolic exothermic oxidation, causing maintenance of the normal temperature (36°C–37.5°C) of the organism’s Internal Energy, generates the greatest quantity of calories promoting suppression of anabolic endoergonic processes in the condition of the treatment by “Prolonged medical Starvation” (during 42-45 days) both in the organism and in cancer tissue. Cancer tissue competes with the organism for use of remained exhausted depot. This competition between the organism and the cancer must lead to the win of most strong one. But the protective forces of the organism will become stronger due to support by herbals extracts of the offered method treatment. In addition, at the beginning of fasting (at 5-7 and 12-14 days) there arises the short acidophilic reaction with formation of ketonic bodies as the result of intensive fat oxidation from fat depots of the organism. As the result of β -oxidation of fat acids many Acetyl ions [CH_3CHO] are produced. The great excess of Acetyl ions increases quantity Acetyl-CoA which promote partial elimination of overload “the nodal point of bifurcation of anabolic and catabolic processes” (symbol NPBac), i.e. elimination of Warburg effect [3,4] (Figure 1). The consumption of Acetyl-CoA by the increased oxidative phase of metabolism (Krebs cycle) causes the decrease of excess lactic acids which accumulate energy for anabolic processes, especially needing for the cancer tissue [3,4]. The elimination of the huge consumption energy and Acetyl-CoA for anabolic processes in cancer metabolism ruins the mechanism of Warburg effect and restores as normal balance

catabolic and anabolic processes as well as the mechanism of Pasteur effect/incompatibility of aerobic processes with glycolysis [3,4]. The elimination of the overload of “Nodal Point of Bifurcation Anabolic and Catabolic Processes” (NPBac) promotes the normal excretion of synthesized high-molecular substances via oxidative processes and ruins the huge excessive Alternative excretion within cells which causes metastasis and non-healing tumour ulcers formation [3,4]. The elimination of the overload of “Nodal Point of Bifurcation Anabolic and Catabolic Processes” (NPBac) restores “contact inhibition of cell propagation” characteristic normal tissue and ruins the irrepressible tumor growth [3,4], keeping the defensive forces of an organism.

Thus basic phenomena of cancer metabolism are inhibited up to destruction of them [3,4].

- a) The mechanism of “Warburg effect”.
- b) Biochemical and biophysical mechanisms of metastases and non-healing tumor ulcers formation.
- c) The phenomenon of “absence inhibition of contact cell propagation in malignant tumor” and as well as irrepressible tumor growth.

These inhibited mechanisms lead to cancer tumor depression, and the light cytotoxic (or cytostatic) effect ruins the metabolism of cancer disease. The light cytotoxic function is carried out possibly by Geranium (or Herb Robert).

The operation of the supporting role extracts of herbs in new method of cancer treatment

Considering the above described mechanism operation of the treatment by “Prolonged medical Starvation during 42-45 days”, this method of cancer treatment leads to depression of development tumor as the result of damage the main mechanisms of cancer tumor metabolism. The shift balance anabolic and catabolic processes into catabolic processes in condition of Prolonged Starvation for maintenance Internal Energy stability of the organism (temperature 36.0°C-37.5°C by which all enzymes operate) displays considerable role of this shift as for survival of the organism as well as for damage the main mechanisms of cancer tumor metabolism, leading to suppression cancer metabolism and to depression of cancer tumor. The crucial role of maintenance Internal Energy stability of the organism in condition of Prolonged Starvation appertains to the all tendered extracts of herbs as well as to the Vegetable Juice Mixture, which deliver to an organism necessary microelements and vitamins, especially Acidum folicum, that is necessary for hemopoiesis, and decreases also acidification in the blood of the organism by “Prolonged medical Starvation”. It must especial pay attention on the extract of red cranesbill (Geranium robertianum) which contains significant amounts of Vitamins A, B and C as well as such minerals: calcium, potassium, magnesium, iron, phosphorus, germanium, according to Isabell [5]. Besides, Breuss notes that red cranesbill (Geranium robertianum) contains the small quantity of radium. Also Isabell notes that Geranium (or Herb Robert) has wide range of clinical applications as remedy with such properties: antibiotic and antiviral properties, sedative property, tonic, astringent, diuretic, digestive, antioxidant. It should be paid attention on especial importance that Geranium (or Herb Robert) is a source of germanium [5] and radium [1,2]. Taking into account that red cranesbill (Geranium robertianum) has antibiotic and antiviral properties [5], it can assume that red cranesbill (Geranium robertianum) has also light cytotoxic property as concern radium which cytotoxic properties do not raise the doubts. Thus it can assume that red cranesbill (Geranium robertianum)

causes light cytotoxic property on depressed malignant tumor in condition of Prolonged Starvation 42-45 days, promoting cancer disease treatment and cure of patient. Such light cytotoxic property can not make negative influence on immune and hormonal systems of an organism essentially as opposed to chemotherapy.

The additional instruction for making “Prolonged medical Starvation 42-45 days”

During the “Prolonged medical Starvation” it’s necessary to look after the common health state of the patient and especially after gastrointestinal tract in order that the patient would have the bowels open timely evacuation of excrements, he would have no constipation (retention of feces). The disturbance of gastrointestinal activity should be healed with vegetable laxatives, activated charcoal, medicaments and use an enema if it’s necessary. The starvation leaving should have taken place during 10 days with gradual addition of used products: juices, then watery decoctions and gels, then vegetable pulps, then baked fruits and vegetables, then liquid kasha (dish of cooked grain), then mashed potatoes, then pair of cutlets-and up to the usual nutrition. The diet shouldn’t be salted during leaving starvation.

The contraindications to the use of the offered method cancer treatment

The irreparable cancerous damage of Internal Medium and, especially, of Internal Energy an organism are the basis of the contraindications to the use of the offered method cancer treatment. So the local excessive shift of balance anabolic and catabolic processes into the huge anabolic processes advances into generalized cancerous process with a plenty of metastasis leading to generalized excessive shift of balance anabolic and catabolic processes into the huge anabolic processes in the organism. The generalized excessive shift of balance anabolic and catabolic processes into the huge anabolic processes via abundant metastasis suppresses catabolic processes of the organism. However just catabolic processes generate energy and dissipate energy into environment promoting maintenance stability energy (36.6°C-37.3°C) for maintenance stability Internal Energy an organism, i.e. catabolic processes contribute to survival of an organism in anti-apoptotic pathways. Thus aggressive processes of metastatic disease promote, on the one hand, the Apoptosis Resistance in cancer cells and, on the other hand, apoptotic processes in an organism. These destructive processes in the organism lead to damage of Internal Energy of the organism, i.e. the states of the organism which symptoms are the contraindication to the use the prolonged medical starvation (42-45 days) of the offered method cancer treatment.

Thus there are the contraindications to the use of the offered method cancer treatment:

* Cachexia is the first cause of contraindication to the use of the offered method cancer treatment, because progressive loss of weight indicates the full downfall of energy forces of the organism and also full downfall of its defensive system, promoting irrepressible development of cancer tumor. Considering such physical state of the organism, the prolonged medical starvation can not deprive cancer tissue of substances for cancer metabolism.

* Full frailty of the organism is the second cause of contraindication to the use of the offered method cancer treatment. This contraindication shows symptoms both unstable equilibrium state of body and helplessness of the person. Full frailty also indicates the full downfall of energy forces of the organism and also full downfall of its defensive system, promoting irrepressible development of cancer tumor.

Considering such physical state of the organism, the prolonged medical starvation can not deprive cancer tissue of substances for cancer metabolism.

* Cancerous intoxication due to the decomposition of cancerous necrotic mass is the third cause of contraindication to the use of the offered method cancer treatment. Cancerous intoxication becomes apparent as sickness, uncontrollable vomiting, anorexia and bad physical state of the organism. Cancerous intoxication indicates irrepressible development of cancer tumor owing to the full downfall of energy forces of the organism and also full downfall of its defensive system. Considering such physical state of the organism, the prolonged medical starvation can not deprive cancer tissue of substances for cancer metabolism.

* Dangerous metastasis for life is the fourth cause of contraindication to the use of the offered method cancer treatment. There are such dangerous for life metastasis: metastasis in brain, metastasis in spinal marrow, vast metastasis in liver causing huge liver and so on.

* The tumors, which create emergency need to urgent medical/ especially surgical help, should not be treated with prolonged medical starvation of the new method cancer treatment before rendering first aid of urgent medical-surgical help. There are such emergency situations: large bowel (colonic) obstruction, urinary obstruction, biliary tract obstruction, airways obstruction, duodenal obstruction, small bowel obstruction, and tumor location in vital center or in vital organs which can be ablated by surgical methods. It is the fifth cause of contraindication to the use of the offered method cancer treatment.

Highlight

The huge anabolic processes with huge consumption of energy and Acetyl-CoA are characteristic for cancer tissue. These processes suppress the catabolic exoergonic processes in cancer tissue retaining only the rest catabolic exoergonic processes for cancer cells survival. The new method cancer disease treatment eliminates excess of anabolic processes in cancer tissue in condition of Prolonged Starvation leading to exhaustion of the organism depots due to the compelled shift balance catabolic and anabolic processes of organism's tissue metabolism into expression of catabolic exoergonic processes for maintenance stability of Internal Energy of the organism (the stable temperature an organism 36.0°C–37.2°C and the other biophysical parameters as pH, osmotic pressure etc., in blood and in neurolymph), that suppress anabolic endoergonic processes characteristic for cancer tissue leading to tumor depression [3,4]. The use light cytotoxic herbal extract in condition of prolonged medical starvation leads to transition of tumor depression into damage of tumor metabolism and to cure of the patient.

Reviews of mechanisms resistance to the cytostatic and cytotoxic effects

Reviews of mechanisms resistance to the cytostatic and cytotoxic effects of drugs in the course of patients treatment, estimating the role of reparative mechanisms in cellular damage caused by cytotoxic drugs. The advantage is combination of the new method to cancer disease treatment with the up-to-date chemotherapeutic therapy.

Describing mechanism of Cordycepin (3'-deoxyadenosine) cytotoxic effect, Imesch et al. [6] researched Cordycepin cytotoxic effect studying both transcription processes, as an inhibitor of Poly (A) Polymerase (PAP), and DNA replication, as MLH1-one of the five DNA Mismatch Repair (MMR) proteins, i.e., processes involved in G2/M phases of cellular cycle. Also they noted that cells with defective

MMR function showed resistance to certain anticancer drugs. So Imesch et al. [6] found that MLH1-deficient tumor cells exhibited reduced susceptibility to apoptosis upon treatment with cordycepin, as compared to MLH1-proficient tumor cells.

Also studying cytotoxic effect of Lipoplatin (a novel liposomal cisplatin exhibiting highly effective against cancers), Fedier et al. [7] revealed that MLH1-deficient tumor cells were less susceptible to apoptosis (i.e. DNA fragmentation) than MLH1-proficient tumor cells. Also they noted that MLH1-deficient tumor cells showed the same sensitivity to lipoxal (a novel liposomal drug-oxaliplatin) as MLH1-proficient tumor cells. The outcomes of Sergeant et al. [8] experiments have led to conclusion that high-level resistance of human colon cancer cells to high doses of cisplatin and oxaliplatin does not seem to be related to acquired defects in the DNA MMR proteins.

However, cancer tissue metabolism is characterized by huge anabolic processes, promoting irrepressible proliferative processes via development G1/S phases of cellular cycle [4]. The development cellular cycle requires mismatch repair (MMR) proteins (enzymes) for reparations of base-base mismatch, that occur during DNA replication in G2/M phases cellular cycle as by MLH1-proficient tumor cells as well as by MLH1-deficient tumor cells. Therefore it can be such case by MLH1-deficient tumor cells that the function reparations of DNA mismatch is distributed as among the all mismatch repair (MMR) proteins (nine genes of MMR function) as well as among the main five genes of MMR function (MLH1, PMS1, PMS2, MSH2, and MSH6). Thus the operative area of the cytotoxic drugs become wider and their cytotoxic effects are divided among these proteins decreasing dosage of cytotoxic drugs on each protein and also decreasing susceptibility to apoptosis upon treatment with these drugs. Only strong cytotoxic drugs with cytotoxic influence on both anabolic processes and catabolic processes in both G1/S and G2/M phases cellular cycle show the similar cytotoxic effects by both MLH1-deficient tumor cells and MLH1-proficient tumor cells.

Besides, remote cellular reactions between cells and cytotoxic drug, which are accomplished by system of cellular capacitors exhibiting interplay between nucleus capacitors, mitochondria capacitors and other organelle capacitors connecting with cellular capacitors, precede contact reactions cells on cytotoxic drugs [9]. Remote cellular reactions set cells to accept the substance of cytotoxic drug. Also remote reactions cells cause attraction between cells and substance of cytotoxic drug which can be weaker in MLH1-deficient tumor cells than in MLH1-proficient tumor cells due to violation in nucleus capacitors influencing on cellular capacitors [9]. Therefore the remote cellular reaction between cells and cytotoxic drug with MLH1-proficient tumor cells can be more absolute than with MLH1-deficient tumor cells. Hence the acting of cytotoxic drug in contact reaction with MLH1-proficient tumor cells can be greater than with MLH1-deficient tumor cells. Thus MLH1-deficient tumor cells can be less susceptible to cytotoxic drug and to apoptosis than MLH1-proficient tumor cells, i.e. drug resistance occurs in MLH1-deficient tumor cells. On the other hand, the interactions between remote cellular reactions and contact cellular reactions show the following sequence of the reactions between cells and cytotoxic drug: Cellular capacitors react on substance of cytotoxic drug and promote attraction cells to cytotoxic drug. Simultaneously mutual interactions between cellular capacitors and nucleus capacitors promote rearrangement Mismatch Repair (MMR) function in nucleus, connecting with molecular structure of cytotoxic drug substance. Such rearrangement Mismatch Repair (MMR) function in nucleus can lead to such case that the operative area of the cytotoxic drug

become wider due to distribution of the function reparations of DNA mismatch as among the all Mismatch Repair (MMR) proteins (nine genes of MMR function) as well as among the main five genes of MMR function (MLH1, PMS1, PMS2, MSH2, and MSH6). Thus the drug cytotoxic effect is divided among the Mismatch Repair (MMR) proteins decreasing dosage of cytotoxic drug on each protein and also decreasing susceptibility to apoptosis upon treatment with this drug.

The advantage of the possible combination very light cytotoxic effect of the small dosages of cytotoxic drugs (Cordycepin, Cisplatin, Lipoplatin, Lipoxal (oxaliplatin) etc.) with the new method cancer disease treatment is that the new method cancer disease treatment leads to depression of cancer tumor metabolism due to suppression anabolic processes, and the cytotoxic effects of the drugs small doses become stronger over the rest of suppressed anabolic processes of cancer tumor in the state of cells depression, showing the similar cytotoxic effects by both MLH1-deficient tumor cells and MLH1-proficient tumor cells due to weak interactions between nucleus capacitors with cellular capacitors in remote cellular reactions.

There are the investigations of the influences of the PI3K/Akt cascade inhibitors on efficiency of cytotoxic effects caused by medical drugs on MLH1-deficient tumor cells or on MLH1-proficient tumor cells:

Ohta et al. [10] and Stathopoulos and Boulikas [11] note that the PI3K/Akt cascade displays an important role in the resistance of ovarian cancer cells to cisplatin: the inhibition of PI3K/Akt increases the efficacy of cisplatin operation.

Fedier et al. [12] investigated dependence of the cytotoxic effect of lipoplatin on AKt inhibitor LY294005. Their outcomes showed that LY294005 inhibitor of AKt decreases the efficacy of cisplatin, lipoplatin, oxaliplatin as well as lipoxal in human colorectal adenocarcinoma, but, unlike these drugs, LY294005 increases the efficacy of Docetaxel and does not affect the efficacy of 6-thioguanine. Fedier et al. [12] prolonged the study of mechanisms AKt inhibition by LY294005 investigating the function of DNA mismatch repair (MMR) in MLH1-deficient tumor cells and in MLH1-proficient tumor cells. The results of researches show that the influence of LY294005 decreases efficiency with Cisplatin and Lipoplatin that is significantly higher in the MLH1-deficient than in the MLH1-proficient, but nearly similar efficiency with Oxaliplatin and Lipoxal. Moreover LY294005 in the MLH1-deficient increases sensitivity with Docetaxel and decrease sensitivity with platinum compounds drugs that can not be associated with the concomitant deletion of the phospho-Aktser473 level. On the contrary, analogous changes in drug sensitivity were observed with the PI3-kinase inhibitor LY294002, but these changes were associated with complete deletion of phospho-Aktser 473. Fedier et al. [12] assume a possible relationship between MMR-mediated with cisplatin DNA damage and action AKt, e.g. a common target for both pathways. Simultaneously Fedier et al. [12] express desire that the possible new property of Akt in making difficulties for drug sensitivity may also be proposed.

Just AKt stimulates glycolysis activating hexokinase 2 (HK-2), i.e. AKt promotes the first an irreversible step in glycolysis, according to Elstrom et al. [13], Gottlob et al. [14] and Ponisovskiy [4] (Figure 1). Besides, Akt promotes growth factor, according to data Plas et al. [15,16]. Just Akt pathway leads to produce Acetyl-CoA via stimulating glucolysis. Thus AKt stimulates both anabolic endoergonic pathway and catabolic exoergonic pathway which are formed from Acetyl-CoA due to "nodal point bifurcation of anabolic endoergonic processes and catabolic exoergonic processes" NPBab [4,5] (Figure 1). Also Cisplatin

and Lipoplatin damage cellular wall violating endocytosis/exocytosis, i.e. they operate in G1/S phases cellular cycle, damaging cellular basis of anabolic processes. Thus they put obstacles in the AKt anabolic endoergonic pathway, retaining only catabolic exoergonic processes with weakened anabolic endoergonic processes. In addition Cisplatin and Lipoplatin also damage nucleus, violating the function of DNA Mismatch Repair (MMR), i.e. they also operate in G2/M phases cellular cycle. Thus mechanisms operations of these drugs show that they more decrease activity in MLH1-deficient tumor cells than in MLH1-proficient tumor cells, because the function reparations of DNA mismatch is distributed in MLH1-deficient tumor cells as among the all Mismatch Repair (MMR) proteins (nine genes with MMR function) as well as among the main five genes with MMR function (MLH1, PMS1, PMS2, MSH2, and MSH6). This distribution occur via DNA replication in G2/M phases cellular cycle because of non-functioned MLH1-deficient tumor cells. Thus the operative area of these cytotoxic drugs become wider and their cytotoxic effects are divided among these proteins decreasing dosage of cytotoxic drug on each protein and also decreasing susceptibility to apoptosis upon treatment with these drugs in MLH1-deficient tumor cells. However Docetaxel exhibits strong anti-mitotic chemotherapy, i.e. Docetaxel violates only G2/M phases cellular cycle. Therefore 'LY294005' in MLH1-deficiency increases sensitivity with Docetaxel due to inhibition of anabolic endoergonic pathway and catabolic exoergonic pathway, which were induced by AKt via glycolysis.

Taking into account these researches it can suppose that the advantage of the possible combination very light cytotoxic effects of the small dosages of cytotoxic drugs (Cisplatin, Lipoplatin, Docetaxel etc.) with the new method cancer disease treatment is that the new method cancer disease leads to depression of cancer tumor metabolism due to suppression anabolic processes, and the cytotoxic effects of the drugs small doses become stronger over the rest of suppressed anabolic processes of cancer tumor in the state of cells depression, showing the similar cytotoxic effects by both MLH1-deficient tumor cells and MLH1-proficient tumor cells due to weak interactions between nucleus capacitors with cellular capacitors in remote cellular reactions.

Also Fedier et al. [17] have researched the influence of HSP90, inhibitor radicicol, on sensitivity to cisplatin in presence of MLH1 protein. Their data demonstrated that radicicol increased the sensitivity to cisplatin and to oxaliplatin in both MLH1-proficient cells and MLH1-deficient cells, but considerably higher in MLH1-proficient cells than in MLH1-deficient cells. However, the increases in platinum drug sensitivity promoting by radicicol, observed in the clonogenic assay, were not accompanied by reproducible alterations in the susceptibility to apoptosis and to changes in cell cycling. Considering data that radicicol is a novel specific inhibitor for heat shock protein 90 (HSP90), they have supposed a possible functional relationship between HSP90 and MLH1, where HSP90 might affect the function of MLH1 in a way that this leads to the counter-regulation of cytotoxic pathways initiated by MMR as a consequence of the presence of DNA damage introduced by cisplatin.

Here is the mechanism decrease generating of energy for maintenance stability of Internal Energy an organism (stable temperature 36.6°C-37.2°C by which all enzymes operate) in condition of high temperature in environment: Catabolic processes of glycolysis carry out peculiar functions, unlike the subsequent catabolic processes after bifurcation of anabolic and catabolic processes in NPBac: Just catabolic processes of glycolysis generate energy. This energy is divided into anabolic and catabolic processes in NPBac, but the part

of this energy is cumulated into Lactic acids for anabolic processes [4]. Thus glycolysis is the primer for both catabolic and anabolic processes. Stimulating glycolysis, AKt pathway is also the primer for both catabolic and anabolic processes. Unlike catabolic processes of glycolysis, the subsequent catabolic processes, which are formed as the result bifurcation of anabolic and catabolic processes in NPBC, dissipate energy into environment for maintenance stability of Internal Energy an organism (stable temperature 36.6°C-37.0°C by which all enzymes operate). The maintenance stability of Internal Energy an organism (stable temperature 36.6°C-37.0°C by which all enzymes operate) in condition of high temperature in environment demands from an organism to suppress generating energy via inhibition glycolysis. Thus the heat shock protein 90 (HSP90) takes part as the link in mechanism inhibition of glycolysis in condition of high temperature in environment, i.e. condition of the heat shock. However the maintenance stability of Internal Energy of an organism (stable temperature 36.6°C-37.0°C by which all enzymes operate) in normal temperature condition occurs via suppression of the mechanism inhibition glycolysis causing by heat shock protein 90 (HSP90) that is achieved via radicicol as inhibitor heat shock protein 90 (HSP90). Therefore it is a possible counter-relationship between HSP90, which inhibits both the anti- and pro-proliferative pathways via suppression of glycolysis, and MLH1, which induces pro-proliferative pathway in G2/M phases cellular cycle. The replicative bypass in drug resistance mediated by loss of MMR can interplay with operations between heat shock protein 90 (HSP90) or p53 which are induced by inhibition of DNA polymerase zeta (anti-proliferative pathways) and Mismatch Repair (MMR) mechanisms (pro-proliferative pathways). Therefore a possible functional counter-relationship between HSP90 and MLH1 functions is demonstrated by HSP90 suppression glycolysis inhibiting both catabolic and anabolic processes in condition of head shock (high temperature in environment) maintaining stable temperature 36.6°C-37.0°C by which all enzymes operate and also suppression MLH1 functions with G2/M phases of cellular cycle. Just it is characteristic for HSP90 to suppress both catabolic and anabolic processes. On the contrary, the function of MLH1 is characterized by maintenance anabolic reparative processes for the advance of G2/M phases of cellular cycle. Therefore, suppressing anabolic reparative processes of the MLH1 function by HSP90 operation, the function reparations of DNA mismatch is distributed as among the all Mismatch Repair (MMR) proteins (nine genes with MMR function) as well as among the main five genes with MMR function (MLH1, PMS1, PMS2, MSH2, and MSH6) that occur via DNA replication in G2/M phases of cellular cycle. Thus the operative area of the cytotoxic property of cisplatin become wider and the cytotoxic effects are divided among the Mismatch Repair (MMR) proteins decreasing dosage of cisplatin cytotoxic effect on each protein and also decreasing susceptibility to apoptosis upon treatment with cisplatin. Just influence of radicicol repairs the Mismatch Repair (MMR) function. Sensitivity to cisplatin is exhibited considerably higher in MLH1-proficient cells than in MLH1-deficient cells due to distribution in MLH1-deficient cells of the drugs cytotoxic effects among the all Mismatch Repair (MMR) proteins, showing more decrease activity in MLH1-deficient tumor cells than in MLH1-proficient tumor cells. Therefore the decrease of MLH1 reparative functions does not change the susceptibility to apoptosis and do not make changes in cellular cycle. Just these investigations confirm the distinction between normal function reparations of DNA mismatch in G2/M phases of cellular cycle and the susceptibility to apoptosis, i.e. resistance to cytotoxic drugs.

The advantage of the possible combination very light cytotoxic

effects of the small dosages of cytotoxic drug (cisplatin) with the new method cancer disease treatment is that the new method cancer disease leads to depression of cancer tumor metabolism due to suppression anabolic processes, i.e. suppression of Mismatch Repair (MMR) function via partial expression HSP90 function. However the cytotoxic effects of the small dose drug (cisplatin) becomes stronger over the rest of suppressed anabolic processes of cancer tumor in the state of cells depression despite of division of the drugs cytotoxic effects among the Mismatch Repair (MMR) proteins with decrease dosages of cytotoxic drug on each Mismatch Repair (MMR) protein.

Meyers et al. [18] have investigated the role of MMR (human MLH1(-) and MMR-deficient HCT116 colon cancer cells) in cellular responses to 5-fluorouracil and 5-fluoro-2'-deoxyuridine (FdUrd). They have determined that HCT116 3-6 cells treated with a low dose of FdUrd had a 2-fold greater G2 cell cycle arrest with MMR-deficient HCT116 cells compared to enhanced G2 arrest in MMR-proficient cells in response to cytotoxic agents.

All these data confirm the possible mechanism counter-relationship between HSP90 and MLH1 in the anti- and pro-proliferative pathways: A low dose of FdUrd had a 2-fold greater G2 cell cycle arrest with MMR-deficient owing to distribution with MMR-deficient HCT116 cells of the drugs cytotoxic effects among the all Mismatch Repair (MMR) proteins due to non-function of MMR-deficient HCT116 cells, unlike MMR-proficient cells in response to cytotoxic agents. Moreover, remote cellular reactions set cells to accept the substance of cytotoxic drug. Also remote reactions cells cause attraction between cells and substance of cytotoxic drug which can be weaker in MLH1-deficient tumor cells than in MLH1-proficient tumor cells due to violation in nucleus capacitors influencing on cellular capacitors [9]. Therefore the remote cellular reaction between cells and cytotoxic drug with MLH1-proficient tumor cells can be more absolute than with MLH1-deficient tumor cells. Hence the acting of cytotoxic drug in contact reaction with MLH1-proficient tumor cells can be greater than with MLH1-deficient tumor cells, in which also the distribution with MMR-deficient HCT116 cells of the drugs cytotoxic effects among the all Mismatch Repair (MMR) proteins due to non-function of MMR-deficient HCT116 cells is occurred. Thus MLH1-deficient tumor cells can be less susceptible to cytotoxic drug and to apoptosis than MLH1-proficient tumor cells, i.e. drug resistance occurs in MLH1-deficient tumor cells.

The advantage of the possible combination with very light cytotoxic effects of a low dose of cytotoxic drug (FdUrd) with the new method cancer disease treatment is that the new method cancer disease leads to depression of cancer tumor metabolism due to suppression anabolic processes, i.e. suppression of Mismatch Repair (MMR) function via partial expression HSP90 function. However the cytotoxic effects of the small dose drug (cisplatin) become stronger over the rest of suppressed anabolic processes of cancer tumor in the state of cells depression despite of division of the drugs cytotoxic effects among the Mismatch Repair (MMR) proteins with decrease dosages of cytotoxic drug on each Mismatch Repair (MMR) protein.

The interest investigations were made by Moreland et al. [19]. They have used Aphidicolin (Ap), an inhibitor of DNA polymerases, to study the role bypass of DNA replication pathway in drug resistance mediated by loss of MMR and received Aphidicolin (Ap) sensitizing drug-resistant cancer cells, that have lost MMR, to bifunctional alkylating and monofunctional methylating agents such as cis-diaminedichloroplatinum II (CDDP) and N'-methyl-N-nitrosourea (MNU).

Just their experiments showed bypass of DNA replication pathway in drug resistance in situation of loss of MMR, i.e. availability for drug resistance. The outcomes of these experiments confirm that the DNA reparative function by loss of MMR and received Aphidicolin (Ap) (an inhibitor of DNA polymerases) occurs via bypass of DNA replication pathway and can be connected as with functional relationship between HSP90 anti-proliferative function and MLH1 pro-proliferative function, as well as with functional condition of cellular capacitors [9] i.e., dependence on cellular remote reactions of cells in mediated drug resistance by loss of MMR and received Aphidicolin (Ap) sensitizing drug-resistant cancer cells via inhibition of DNA polymerases, i.e. the above described mechanisms.

The advantage of the possible combination very light cytotoxic effects of the small dosage cytotoxic drug with the new method cancer disease treatment is that the new method cancer disease leads to depression of cancer tumor metabolism due to suppression anabolic processes, i.e. suppression of Mismatch Repair (MMR) function and expression HSP90 function, that was exhibited in the Moreland et al. [19] experiments with the mediated drug resistance by loss of MMR and received Aphidicolin (Ap) sensitizing drug-resistant cancer cells via inhibition of DNA polymerases. However the cytotoxic effects of the small dose drug become stronger over the rest of suppressed anabolic processes of cancer tumor in the state of cells depression despite of division of the drugs cytotoxic effects among the Mismatch Repair (MMR) proteins with decrease dosages of cytotoxic drug on each Mismatch Repair (MMR) protein.

Also Lin and Howell [20] experiments exhibit that DNA Mismatch Repair (MMR) function and p53 function are major determinants of the rate of development of cisplatin resistance: Loss of either MMR or p53 alone increased the rate of development of resistance to cisplatin. Simultaneously inhibition of DNA polymerase zeta by suppression of the expression of REV3 subunit eliminates the increased rate of development of cisplatin resistance observed in the MMR-deficient cells. Similar data, concerning influences of DNA mismatch repair and p53 function on the rate of development of multitude cytotoxic drugs resistance, were received by Lin et al. [21] and Yanamadala and Ljungman [22] have expressed opinion that MMR proteins can bind to certain DNA lesions and signal p53 and apoptosis by an unknown mechanism, using both alkylating agents and H₂O₂ which caused significant inhibition of mRNA synthesis in MLH1-expressing but not in MLH1-deficient cells. They suggest a novel mechanism of MLH1 in the induction p53 and apoptosis by inhibiting RNA polymerase II-dependent transcription on damaged DNA templates.

Moreover Stubbet et al. [23] indicate that the Transcription Coupled-Nucleotide Excision Repair (TC-NER) play a prominent role in determining the sensitivity of tumour cells to cisplatin even in the absence of p53 and DNA mismatch repair.

DNA polymerase zeta takes part in somatic hypermutation of immunoglobulin genes, i.e. pathologic anabolic processes. Unlike DNA polymerase zeta, the Mismatch Repair (MMR) function and p53 prevent pathologic anabolic processes of excessive proliferative processes, expressing development of normal cellular cycle via maintenance balanced interactions between anabolic and catabolic processes in G2/M phases of cellular cycle. Thus expression DNA polymerase zeta and expression Mismatch Repair (MMR) function or p53 cause different chemical potentials (μ) which create the cellular capacitors with inverse cellular operations [9]. Therefore inhibition DNA polymerase zeta eliminates the increased rate of development of cisplatin resistance observed in the MMR-deficient cells. On

the contrary, loss of either MMR or p53 alone increases the rate of development of resistance to cisplatin.

The advantage of the possible combination very light cytotoxic effects of the small dosage cytotoxic drug with the new method cancer disease treatment is that the new method cancer disease leads to depression of cancer tumor metabolism due to suppression anabolic processes, i.e. suppression either Mismatch Repair (MMR) function or p53 function of tumor suppression. The suppression either Mismatch Repair (MMR) function or p53 function of tumor suppression causes distribution of the drugs cytotoxic effects among the all Mismatch Repair (MMR) proteins. However the cytotoxic effects of the small dose drug become stronger over the rest of suppressed anabolic processes of cancer tumor in the state of cells depression despite of division of the drugs cytotoxic effects among the Mismatch Repair (MMR) proteins with decrease dosages of cytotoxic drug on each Mismatch Repair (MMR) protein.

Investigating an interesting class of anticancer agents Minor Groove Binders (MGBs), Fedier et al. [24] have selected Brostallicin which is a synthetic O \pm bromoacrylic MGB. DNA Minor Groove Binders (MGBs) are a class of anticancer agents highly effective in a variety of human cancers. Just the outcomes of their researches reveal that brostallicin-induced cytotoxicity does not depend on functional DNA MMR. Besides, Fedier et al. [24] noticed that Brostallicin does not alkylate DNA *per se* but through the interaction with GSH/GST system. After all tumour cells are characterized with higher Glutathione (GSH) and Glutathione-S-transferase (GST) levels, according to data Geroni et al. [25]. Moreover Glutathione (GSH) is found in cellular wall and DST enzyme catalyzes GSH peroxidase activity, that lead to the detoxification of lipid and nucleic acid hydroperoxides, according to data Waxman [26]. Also Waxman [26] noticed that DST enzyme exhibit a ligand binding function, which involves the non-covalent binding such substrate as heme, bilirubin, various steroids, and some lipophilic anticancer drugs.

These investigations show that cytotoxic effects of Minor Groove Binders (MGBs) of Brostallicin does not depends on DNA Mismatch Repair (MMR) mechanisms [24], and the cytotoxic effect MGB occurs through GSH/GST system of cellular wall and cytoplasm [25,26]. Just the changes in GSH/GST system of cellular wall and cytoplasm, caused by cytotoxic effects via Minor Groove Binders (MGBs) of Brostallicin, change as chemical potentials (μ) as well as the cellular capacitors [9] which do not depend on DNA Mismatch Repair (MMR) mechanisms. Thus the cytotoxic effects of Minor Groove Binders (MGBs) of Brostallicin take part in cellular remote reaction via GSH/GST system of cellular wall, involved in cytotoxic processes, and cytoplasm. The cellular remote reaction precedes contact reaction [9], as for recognizing substance of cytotoxic drug as well as for processes of resistance to cytotoxic drug which do not depend on DNA Mismatch Repair (MMR) mechanisms.

The advantage of the possible combination very light cytotoxic effects of the small dosage cytotoxic drug with the new method cancer disease treatment is that the new method cancer disease leads to depression of cancer tumor metabolism due to suppression of anabolic processes. The remote cellular reactions between depressed cells of cancer tumor and cytotoxic effect of Brostallicin, which are accomplished by system of cellular capacitors exhibiting interplay between nucleus capacitors, mitochondria capacitors and other organelle capacitors connecting with cellular capacitors, precede contact reactions cells on cytotoxic drugs [9]. Remote cellular reactions set cells to accept the substance of cytotoxic drug and cause attraction

between cells and substance of Brostallicin [9]. However remote reaction of depressed cancer cells in condition of prolonged medical Starvation of the new method cancer disease treatment is violated and would not be able to cause drugs resistance. However the cytotoxic effects of the small dose Brostallicin in contact reaction become stronger over the rest of suppressed anabolic processes of cancer tumor in the state of cells depression despite of division of the drugs cytotoxic effects among the Mismatch Repair (MMR) proteins with decrease dosages of cytotoxic drug on each Mismatch Repair (MMR) protein. These mechanisms don't damage immune and hormonal systems and don't cause drug resistance.

Highlight: The chemotherapeutic mechanisms of all anticancer drugs are directed to damage regulating system (enzymes, cellular capacitors, etc.) for inhibition or damage of proliferative anabolic properties of cancer cells, that causes damage to proliferative properties of anabolic functions of an organism's immune and hormonal system (defensive mechanisms an organism) and violation of Internal Energy and Internal Medium an organism. Unlike chemotherapy, the inhibition of proliferative anabolic properties of cancer cells is achieved via the rearrangement of cancer metabolism from anabolic pathway into catabolic pathway in the offered new method cancer treatment by Prolonged Starvation with very small dosage cytotoxic herbal extract. Thus the offered new method cancer treatment puts cancer metabolism into state of depression and preserves proliferative anabolic functions of an organism's immune and hormonal system (defensive mechanisms an organism) and Internal Energy and Internal Medium an organism. The new method of cancer treatment shows such mechanisms: Prolonged medical Starvation put cancer metabolism into depression, and the light cytotoxic effect of very small dosage cytotoxic herbal extract in condition of cancer depression causes damage of cancer cells and recovery of oncologic patient. Also this light cytotoxic effect in condition of cancer depression does not induce mechanism of drugs resistance, preserving defensive mechanisms an organism (immune and hormonal system).

Discussion of advantage possibility combinations the up-to-date methods cancer treatment with the new method cancer treatment

This article is continuation of the article entitled "The new method cancer disease treatment making the rearrangement of metabolism from pathological development into normal development", which was accepted for publication in "Journal of Clinical Trials". Just the result of treatment by the offered new method cancer disease treatment and discussion concerning this method treatment were described in the article entitled "The new method cancer disease treatment making the rearrangement of metabolism from pathological development into normal development". Prolonging data of the article entitled "The new method cancer disease treatment making the rearrangement of metabolism from pathological development into normal development", it was described in this article combination of the applied herbs extracts for the treatment of the patient, methods of preparation extracts from the herbs and the method of application of these extracts for cancer treatment and was made detailed description and explanation the mechanisms of the offered herbs extracts operation, that can help to practical application of the new method cancer treatment and advance researches of possible integration of the offered method cancer treatment with up-to-date methods cancer treatment after detailed Clinical Trials. Also it was prolonged investigations mechanisms of drug resistance: So the mechanisms of changes in an organism metabolism as the result of the long anticancer treatment, leading to drugs resistance

and causing multiple cancer disease remissions were studied in the article entitled "The new method cancer disease treatment making the rearrangement of metabolism from pathological development into normal development", and the mechanisms of changes in an organism metabolism, which result in drug resistance in the course of patient treatment, were studied in this article. Significance of both these articles is like this: Interpreting the outcomes of experiments, studying mechanisms resistance to the anticancer drugs, there were offered the explanations of the mechanisms anticancer drugs resistances, as the result of the long anticancer treatment as well as drug resistance in the course of patient treatment. Evaluating the offered mechanisms of the drugs resistances, it was presented the advantage of the tendered new method cancer disease treatment over the up-to-date methods cancer treatment and was offered the eventual modes of combination the offered new method cancer disease treatment with modern chemotherapeutical methods cancer treatment after detailed Clinical Trials. Thus the described action of the extracts of herbs in condition of Prolonged Starvation in the new method of cancer treatment demonstrates combined treatment causing both suppression anabolic endoergonic processes of cancer metabolism, which leads to depression of cancer tumor, and light cytotoxic influences on cancer cells, which leads to full destroy of cancer metabolism with cure of a patient. Such mechanism of cancer therapy by the new method of cancer disease treatment contributes to assume eventual combinations of the new method cancer treatment with the modern methods cancer treatments. The surgical methods of treatment are often preferable methods in combination with the described new method of cancer treatment. Just it is often necessary to ablate the tumor, making resection of it, in cases the excessive increase in the size of the tumor when the tumor is capable to compete with the organism for use the rests of the organism depot in the conditions of Prolonged Starvation 42-45 days. Also surgical treatment is necessary in cases when there is a danger for life of the patient. Supplementary combination of the described method treatment with the other modern methods treatment (Chemotherapy, Roentgen-therapy and Radiotherapy) can be applied considering the phase of tumor state during the treatment by Prolonged Starvation 42-45days. The tumor falls into the depression as the result of the treatment by Prolonged Starvation 42-45 days. The restoration of the tumor state lags behind the organism restoration in the stage of leaving starvation especially. Thus it is necessary to evaluate influences on an organism of Chemotherapy and to determine in what phase of the new method treatment by Prolonged Starvation 42-45 days it is possibility to apply the modern methods and to determine the minimal effective dosage of applied medical drugs. Besides it is possible to assume that combination of treatment by the modern medical drugs with the offered new method cancer disease treatment by Prolonged Starvation 42-45 days would be carried out by considerably smaller dosage of modern medical drugs. Thus the possible modes to integrate the offered method cancer treatment with the modern methods cancer treatments should be made after detailed Clinical Trials. The rational combination of the new method of cancer disease treatment with modern methods of cancer therapy must accelerate recover of oncologic patients.

Conclusions

1. Inflows of substances and energy from the common sources/ spots of an organism/both in the organism and in the tumor in condition of prolonged medical starvation are the first feature of the new method of cancer treatment.
2. The shift of balance catabolic and anabolic processes of the organism Internal Medium into catabolic processes in the condition of

the organism depot exhaustion owing to prolonged medical starvation for maintenance of stability of the organism Internal Energy, which is necessary for an organism surviving, is the second feature of the new method of cancer treatment.

3. The shift of balance catabolic and anabolic processes of the organism Internal Medium into catabolic processes in the condition of the organism depot exhaustion owing to prolonged medical starvation causing shift of the tumor metabolism into a catabolic pathway with damage of an anabolic pathway, characteristic for tumor, results in damage of tumor metabolism and Warburg effect leading cancer metabolism to depression, that is the third feature of the new method of cancer treatment.

4. The very light cytotoxic herbal effect in condition of cancer depression causes damage of cancer metabolism, leading to recover of oncologic patient.

5. The very light cytotoxic herbal effect in condition of cancer depression does not violate defensive mechanisms an organism (immune and hormonal system) and does not induce mechanism of drug resistance unlike chemotherapeutic methods of cancer disease.

6. Advantage of a new method of cancer treatment over modern methods of chemotherapy is that maintenance of stability of the Internal Energy and Internal Medium an organism is not broken in the conditions of prolonged medical starvation of the new method of cancer treatment, unlike up-to-date chemotherapeutic methods of cancer disease.

7. Hormonal regulatory processes and protective immune processes of the organism is preserved by new method cancer treatment in comparison with damaging of metabolic links of anabolic processes both in the organism Internal Medium and in the tumor causing violation of hormonal regulatory processes and protective immune processes in an organism by up-to-date cytotoxic/or cytostatic methods of treatment.

8. It was offered the possible combination the new method of cancer treatment with the up-to-date methods of cancer treatment which should be used after detailed Clinical Trials.

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