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THE BIOMAGNETIC NATURE OF CANCER AND THE ROLE OF POTASSIUM ASCORBATE AND RIBOSE AGAINST CELLULAR DEGENERATION

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ABSTRACT

Free radicals are the main cause of cell oxidative stress, and can induce cell degeneration, DNA mutation, and carcinogenesis. A free radical is a paramagnetic cation because it is an atom or molecule with uncompensated magnetic moment. Due to this, the magnetic fields generated by free radicals can play a crucial role in influencing the direction and the course of redox chemical reactions. According to our data, we think that, at the cellular level, the first step of the oxidative stress is the damage to the Na/K pump, and this can induce an electrolytic imbalance with a potassium efflux from the cytoplasm. This fact is so dramatic for the cell that a chain of events can start that leads to a process of degeneration. Indeed, some works about the activation of apoptosis have put in evidence that potassium plays a primary role as the main regulator of cellular metabolism.

Potassium ascorbate (a vitamin C-derived salt) and ribose can quickly transfer K to the intracellular level and balance its concentration, working on the heterocyclic groups of proteins and enzymes like pyrrolic and furanoid rings. Our data confirms that this compound is also effective to protect cells from oxidative stress, and it shows an antimutagen behavior.

INTRODUCTION

Oxidative processes are involved in promoting and developing cancer [1-3]. The main cause of oxidative stress is free radicals. These are one-unpaired-electron molecular fragments created by the unimolecular dissociation of excited states and of radical ions. Free radicals are paramagnetic substances; they continuously develop in living organisms and continuously enter into reactions producing definite compounds. Their basic properties are high chemical reactivity as well as a relatively short lifetime when in the free state.

A living organism tends to maintain constant the free radical concentration just to guarantee normal biological processes. From the magnetic point of view, their uncompensated spins must be counted because their high reactivity is connected with their paramagnetic properties.

The main causes underlying the development of free radicals from magnetically neutral molecules are:

- external energy absorption;
- induction of a molecular decomposing reaction;
- induction of an electron transfer reaction.

It should be noted that even the magnetic field generated by a nuclear magnetic moment can modify chemical reactions, reversing the direction of chemical reactions and influencing metabolic processes [4].

It is our opinion that the oxidative stress damages the structure of the cellular membrane, primarily the sodium-potassium ATP-ase, first of all. This fact induces a heavy alteration of the active transport mechanism between sodium (Na) and potassium (K), and it modifies oxide-reduction reactions between cytoplasmatic molecules. We think that these events are the biochemical 'trigger' for cancer. In fact, potassium is a critical regulator for cell metabolism control, as evidenced in cellular apoptosys [5-9]; it is the main cytoplasmatic cation (co-factor), and it acts like a catalyzer with enzymes and proteins [10] through a particular process called reversible salification of the aminic (NH_2) groups in a subacid environment. Moreover, some aminoacids (hystidine, proline, triptophane) have in their lateral chain a pyrrolic group in which the ethero-atom is composed of an NH group. This ring has a subacid pH mostly close to the NH group and, in this particular condition, the potassium is able to salify in a reversible way the iminic group substituting the hydrogen atom. We can note that the local pH change, as well as the presence of oxidants, is able to destroy the aromatic character and open the pyrrolic ring. So this salification is no longer possible and K cannot execute its task.

In basic physiological conditions (or, as we say, 'at rest'), K is a cation mainly present inside the cell at concentrations on the order of 150 mmol/l, while on the extracellular side, concentration is approximately 5 mmol/l. The cation sodium, which plays a fundamental role for the hydro-balance of the organism and has high chemical affinity with potassium, behaves in exactly the opposite way with respect to K: it is mainly present in extracellular area to the order of 150 mmol/l, whereas at the intracellular level, it is on the order of 5 mmol/l. In this way the two cations have a high concentration gradient between the inside and the outside of the cell. These two cations play a crucial role in nerve conduction and in the mechanism of sensory perceptions.

In the late 1930's, the two scientists Moraveck and Kishi, Hungarian and Japanese respectively, conducted some experiments on some types of tumors. Studying particularly the Rous sarcoma, they measured the loss of intracellular potassium. Their studies showed that this loss through the cytoplasmatic membrane allows the emission of sodium with a ratio that increases proportionately to the cellular degradation increase [11]. This fact seems to be the main characteristic of all types of tumors, confirmed also through simple electrolyte blood tests. Our Foundation normally requires such tests from cancer patients.

Probably the cause of this process should be put in relationship with the 'degradation' (that is to say 'opening') of pyrrolic rings in enzymes and proteins, thus making them unable to conduct their own biologic activity, and local pH modification, thus avoiding the reversible salification processes. In these conditions the intracellular potassium goes out of the membrane by simple diffusion, which increases at a par with the damage done to the pump. Simultaneously, by the same diffusion mechanism, sodium starts to cross the membrane in the opposite direction going into the cytoplasm. This mechanism is very dangerous for the cell because:

- It starts a temporary, as well as lasting, transfer of calcium from intracellular deposits (for example the mitochondrion), that could be jointly responsible for the mithogenic stimulation;
- The glucose and the sodium are transported simultaneously into the cytoplasm; this movement increases with the sodium-potassium pump breakdown.

These reactions induce the cell to modify its own respiration process, in such a way that it reduces the oxidative phosphorilation and improve glicolysis (that is to say fermentation) substantially. A high production of lactic acid formed by piruvate reduction ensues. Stating that the piruvate is an inhibitor of mitosis, S phase starts up, its constant decrease into cytoplasm (due to the convertion into lactic acid) takes out this block over mitosis, directing the cell metabolism to uncontrolled proliferation. The intracellular pH is modified, tending to alkaline, and also cellular respiration is modified with a consequent considerable change of the 'Krebs cycle' [12].

All these reactions induce the destruction of the aromaticity of the ribose furanoid ring in the RNA; so the same RNA tends to polymerization, discharging stronger Van der Waals forces over the nucleus with a consequent transfer of wrong information from the 'peripherial side' to the 'headquarters' (the DNA) [13-14]. In this way the nuclear DNA undergoes mutation that leads up to carcinogenesis.

Potassium Ascorbate (CK) and Ribose (R) are able to counteract this process, protecting the cell against oxidative stress and fighting the uncontrolled proliferation process, as evidenced thanks to a research plan conducted by the Pantellini Foundation together with Prof. Ida Ortalli, Dr. Simonetta Croci, and their colleagues of the Public Health Dept., University of Parma, Italy [15-16]. Italian biochemist Dr. Gianfrancesco Valsé Pantellini was the scientist who discovered these properties of the compound and the compound's surprisingly positive effects against cancer [17-18].

Ascorbic Acid (Asc) is a very powerful anti-oxidant and a very important vitamin for the human organism [19-20]. It is a penta-sugar with a furanoid structure (like Ribose), thus the ring responsible for biological activity is very similar to the pyrrolic one (it has oxygen as hetero-atom). CK is derived from the salification in subacid of the hydrogen atom within the Asc OH groups into the furanoid ring.

Ribose is the sugar more strictly connected with nucleotide biosynthesis. It is an integral part of the cell, and it plays a fundamental role in the cell's energetic metabolism. In particular it is a fundamental precursor of the RNA biosynthesis as well as of adenosine (which is an essential component in the production of ATP and is strongly involved with Na/K ATP-ase). When it is consumed orally, it is metabolized and does not interfere with glycolysis [21]. The use of a specific quantity (2%) of Ribose compared to Asc together with Potassium Ascorbate (RCK) and in the form of Potassium Ribosate (RK) can be explained by the potential catalytic activity of Ribose for the purpose of improving the compound efficacy.

In order to know with more accuracy the action mechanism of these compounds, and to evaluate their protective action, the properties of CK and RCK are investigated with short-term tests to establish their possible antimutagenic behavior. For this purpose, thanks to a research plan conducted by the Pantellini Foundation together with Prof. Giorgio Bronzetti and Dr. Clara Della Croce, of the Institute for Biology and Agricultural Biotechnology, National Council for Research (CNR) of Pisa (Italy), D7 strain of yeast *Saccharomyces cerevisiae* are employed as an eucaryotic genetic system; it constitutes a rapid, inexpensive and reproducible model that can be correlated also to a potential carcinogenetic effect. Moreover, its genome is completely sequenced [22] and 50% of yeast proteins seem to have significant levels of homology with human proteins.

METHODS AND RESULTS

Potassium Ascorbate (CK) is a Vitamin C-derived salt that is totally non-toxic and does not present any side effect. This salt is obtained as a reaction product of Asc salification (150 mg) in 20 cc of water by 300 mg of potassium dicarbonate ($KHCO_3$) at room temperature. These components should have a crystalline form of not less than 97% purity. The solution can be used for a long time, and it follows biologically the destiny of the ascorbic acid. In view of the low level doses and the non-toxic effects of this compound, potassium ascorbate has been used on man directly, to evaluate its effects on neoplastic pathologies.

This compound was given three times a day on an empty stomach:

- in the morning 20 minutes before breakfast;
- 45 minutes before lunch and 45 minutes before dinner.

The data *in vivo* refer to 1,200 samples of patients with different types of cancer, and they are reported by local practitioners only. This was due to the fact that, as a biochemist, Dr. Pantellini could neither visit patients nor keep their medical file. It follows that this data is not statistically homogeneous and it refers only to the quality of life and the staying alive.

All patients were in a very advanced tumoral phase; nearly 70% of them were in the so-called 'terminally ill phase', and clinical and normal basic assistance had exhausted their possible remedies, the only thing to do for them was therapy against pain. The remaining 30% was made up of patients who, after surgical interventions and/or radiotherapy or chemotherapy, had decided to stop all treatment as per medical advice.

In Fig.1 it is possible to observe a first significant element concerning the survival capability after 5 and 10 years from CK consumption by the patients. One has to keep in mind that people with very advanced oncological phases are being studied.

Comparing the survival rate capability of the patients after 5 and 10 years of CK treatment, we come to the interesting conclusions that, unexpectedly, these sets of data are not very different from each other; it seems that patients able to survive up to 5 years can reach the 10 years level and even more.

Fig. 2 is shows the range of symptom variability in a group of 30 patients affected by different types of cancer. It is possible to observe within 60 days, as an average value, that symptoms largely decrease and the patient' quality of life does improve radically.

Prof. Bronzetti, Dr. Della Croce and their group of the National Council of Research in Pisa, Italy, have used a D7 strain of yeast *Saccharomyces cerevisiae*, obtained from F.K. Zimmermann, and they have measured Survival (S) and Point reverse Mutation (PM) [23] after incubation with AcetilPhenylHydrazine (APH) as oxidant to evaluate antimutagenic effect induced by CK and RCK.

Cellular culture: About 10^7 cells/ml have been inoculated in liquid complete medium containing 2% glucose, 2% bactopeptone and 1% yeast extract, and incubated at 30°C for 48 h up to the stationary phase (100 x 10^6 cells/ml) (S).

Growing test procedure: To perform these experiments, CK and RCK at nM (nano-molar) concentrations were added in the liquid medium during stationary growth phase. Cells were counted to evaluate cyto-toxicity during growth and then plated, after suitable dilutions, on complete and selective media to ascertain survival and revertants.

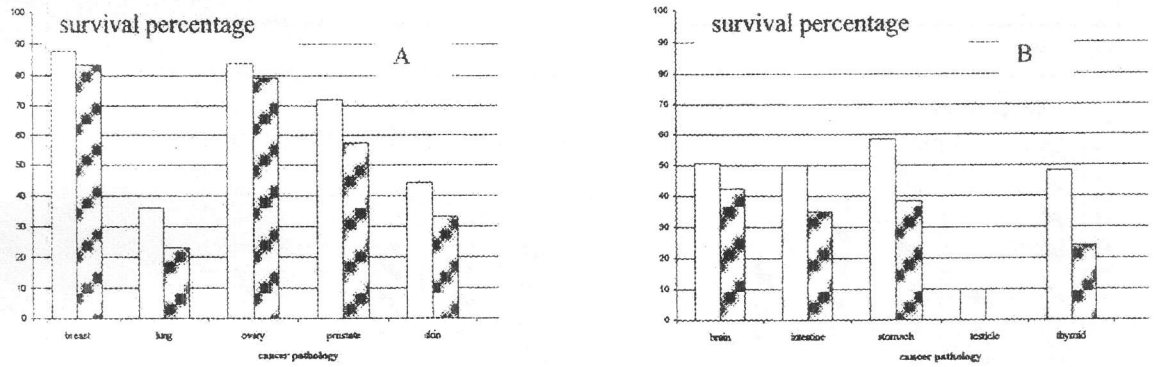

Figure 1. In A and B are represented the cancer pathologies *vs.* survival percentage at five years (white bars) and ten years (striped bars). Testicular cancer in B represents an exception in the data due to a very low number of patients and to the particular aggressiveness of this syndrome in its advanced phases.

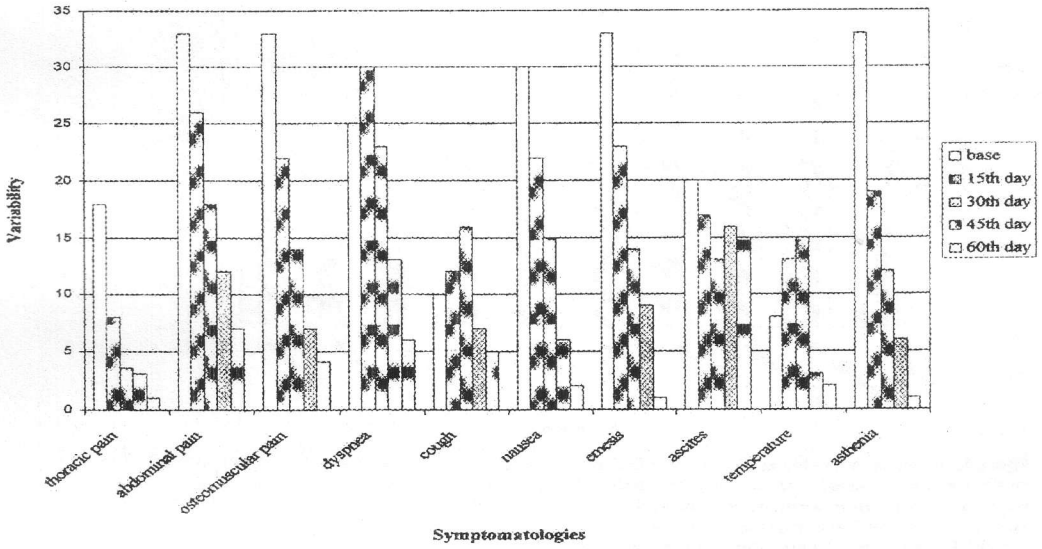

Figure 2. Symptom variability in a neoplasia mixed group. On the X-axis are reported all the symptomatologies, while on the Y-axis are reported arbitrary numbers obtained through normalizing criteria. In point of fact, not all symptoms can be measured with instruments; therefore it is necessary to adopt numeric criteria of evaluation for the symptoms, known as psychometrical or psychophysical scales, which are either visual and/or analogic. Having adopted the starting criteria, data is rendered homogeneous through normalizing procedures.

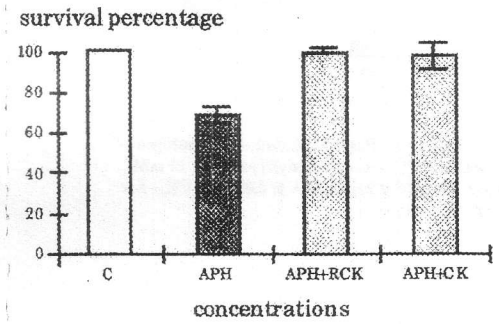

Figure 3. Growing Test: Survival – Antimutagenesis. C – Control; APH – AcetilPhenylHydrazine 10 mM; RCK – Asc 3 nM + $KHCO_3$ 6 nM + R 0.06 nM; CK – Asc 3 nM + $KHCO_3$ 6 nM.

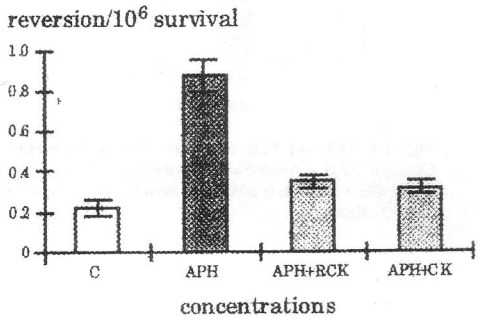

Figure 4. Growing test: Point Mutation – Antimutagenesis. C – Control; APH – AcetilPhenylHydrazine 10 mM; RCK – Asc 3 nM + $KHCO_3$ 6 nM + R 0.06 nM; CK – Asc 3 nM + $KHCO_3$ 6 nM.

Results have been statistically analysed using the Analysis of Variance.

Figure 3 shows the effects of CK and RCK on survival percentage rates in growing cells of D7 strain of yeast *Saccharomyces cerevisiae* after an overnight incubation at 30 °C with APH.

Figure 4 shows the effects of CK and RCK on Point Reversion Mutation in growing cells of D7 strain of yeast *Saccharomyces cerevisiae* after an overnight incubation at 30 °C with APH.

We can see that CK and RCK recover significantly the decrease of Survival percentage and reduce significantly the increase of Point Mutation due to APH.

DISCUSSION:

The extremely promising data clearly demonstrates that CK and RCK show a real effect against cancer *in vivo*, and an antimutagenic behavior *in vitro* on yeast *Saccharomices cerevisiae* at nM concentration. These facts can be related to the carrier properties of Asc as a consequence to its own specific and heterocyclic structure, allowing a fast K intracellular transfer. I think that this characteristic of Asc carries out the main role in CK and RCK together with its antioxidant action. Moreover, I am also convinced that Ribose could inhibit the RNA polymerization process during the cellular degenerative process, salifying potassium in a way analogous to that of Asc.

The presence of K in cancer cell can induce the related effect of removing Sodium (and also glucose, for the sinport explained in the introduction) from the intracellular region. So, this presence produces:

- a new modification in local intracellular pH;
- a fast lowering of the nutritive reserves, reducing glicolysis and reintroducing a block over mitosis; in this way it is possible to inhibit the uncontrolled proliferation

This data could suggest what we might expect from the CK and RCK therapy, as well as how the assumption of these compounds can really produce significant benefits in the struggle against cancer.

In fact, CK and RCK can operate at different levels:

- at the prevention level by maintaining the correct concentration of electrolytes and improving the cellular metabolism;
- in the presence of cellular degenerative risk by offering to the cell a protective system and adjusting the electrolytic imbalance,
- in the presence of tumoral attack, making the environment asphyxial for tumoral cells.

In conclusion, the further consideration of this job is that degeneration does not start from direct damage to nuclear DNA, but from a cytoplasmatic anomaly; that is to say, the damage comes from the 'peripherial side'. This means that DNA functionality can be strongly influenced by different components (especially different types of RNA), by the internal cellular environment, and also by cell-cell communications.

It is evident that this hypothesis, if confirmed, could alter the basic principles of molecular biology, which can be summed up in the 'central dogma'. Nevertheless, it is my opinion that we have to follow this new road in our quest to understand better the 'cancer question' and its possible solutions.

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