POSITRONIUM ATOM IN SOLUTIONS: THE POSSIBILITY OF QUICK DIAGNOSTICS OF CARCINOGENIC HAZARDOUS COMPOUNDS

L.I. Zemskaya, M.P. Ivanova, A.S. Borisov, S.V. Stepanov, A.A. Fenin

National Research Center "Kurchatov Institute", Institute for Theoretical and Experimental Physics

D. Mendeleyev University of Chemical Technology

It is generally accepted that chemical carcinogens are the main source of cancer. When these substances enter the body, they cause the formation of malignant tumors (uncontrolled dividing cells that can grow into neighboring tissues and organs. Being in cells, carcinogens may cause genetic changes: damage in the structure of DNA, in their replication, loss of a part of chromosomes etc. As a result, hereditary changes (mutations) may appear. This is the beginning of the oncological process. Positron annihilation time spectroscopy can be used as one of the physicochemical methods to determine the carcinogenic activity of chemical compounds.

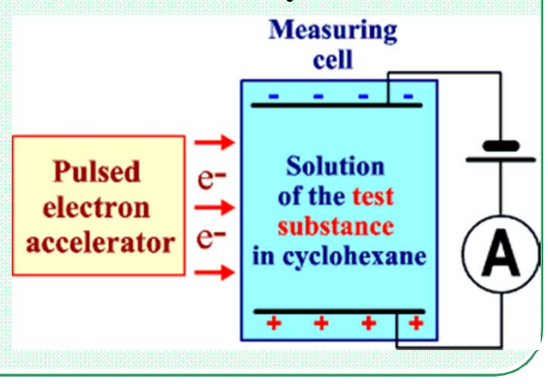
More than 60 years ago, the spouses James and Elizabeth Miller established that the main feature of carcinogens is their high affinity for the electron (electrophilicity).

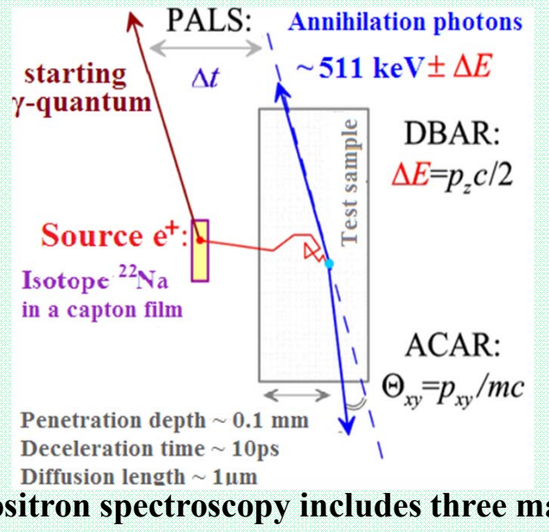
Once in the cell (in the aquatic environment), some carcinogens (genotoxic) form chemically active derivatives containing an electrophilic group. This group forms strong covalent chemical bonds with DNA molecules.

As a result, the accuracy of cell genome reproduction is impaired, DNA replication is disrupted, mutations arise, and carcinogenesis begins.

Other carcinogens (procarcinogens) acquire carcinogenic (electrophilic) properties as a result of biochemical transformations within the body (metabolic activation). Using the Millers' idea, George Bakale (Case Western Reserve University, Ohio, USA) proposed to measure a quantity related to electrophilicity, the rate constant of the capture of an excess electron in experiments on pulsed radiolysis (80s of the last century).

He measured several hundred trapping rate constants of e^- by various substances in cyclohexane $k(e^-+S)$. It was shown that if $k > 3*10^{12}$ $M^{-1}s^{-1}$ (this is the rate constant of e^- capture by CCl_4), so this test substance is a carcinogen with 85% probability. However, to implement Bakale's method, a complex setup is required, including an electron accelerator with an energy of several MeV and a cumbersome γ-shielding.





Our proposal is to use the lifetime positron annihilation spectrometer. This technique is similar to the G.Bakale method, but turns out to be simpler, more compact, and does not require much γ-shielding.

The essence of the positron spectroscopy consists in the injection of e+ into the solution under study and in the subsequent registration of the emitted γ-quanta.

Positron spectroscopy includes three main methods:

1) lifetime (measuring the positron lifetimes before annihilation);

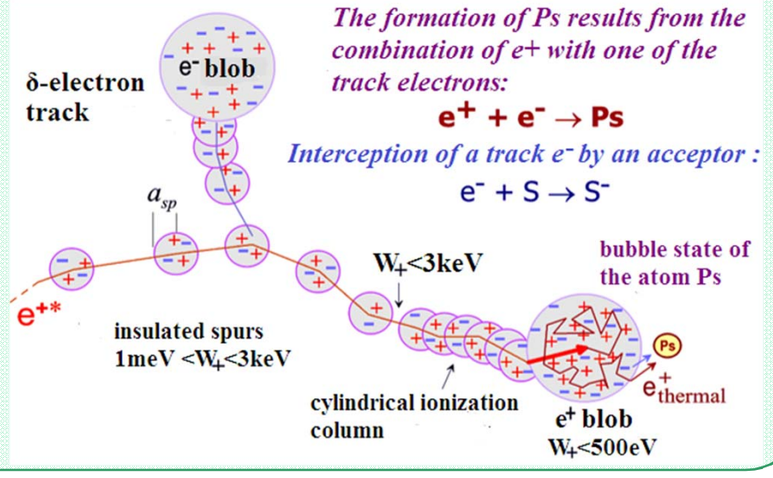
2) angular (measuring the deviation of the scattering angle of annihilation photons from 180°)

3) Doppler (measurement of the energy of the annihilation γ-quanta).

Track structure of the fast e+ in liquids

- e^+ penetration depth - 1-3 mm
- e^+ slowing down time - 5-10 ps
- probability of the Ps formation - 30-50%
- ortho-Ps lifetime - several ns

Dissolving of a scavenger S of the track electrons suppresses the Ps yield!



In PAS the radioactive nuclei (e+ source) play a role of the "accelerator". Flying into the medium under study, energetic positrons form tracks and generate secondary electrons. If an investigated substance, being dissolved in the medium, effectively captures track electrons, so the Ps yield will decrease.

In positron experiments, we measure inhibition coefficients of Ps formation by various solutes and use these coefficients as a measure of the carcinogenicity of the test substances.

Consequently, it is necessary to understand the mechanism of Ps formation and to have a model that describes:

track e- capture by the testing molecules (inhibitors or anti-inhibitors)

$$e^- + S \rightarrow S^-, \qquad e^- + A \rightarrow A^-,$$

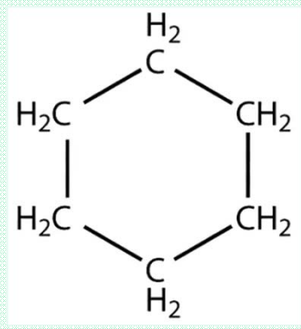
solvation of e- and e+

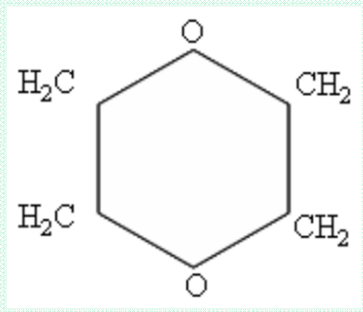
$$e^- \rightarrow e^-_{solv}, \qquad e^+ \rightarrow e^+_{solv},$$

the Ps formation through combination of a positron with one of the track electrons, as well as a result of the e- detachment of a weakly bound anion A-

$$e^+ + e^- \rightarrow Ps, \qquad e^+ + A^- \rightarrow Ps + A.$$

According to the Miller hypothesis, carcinogens (strong electrophiles) should efficiently inhibit Ps formation. Initially, we planned to conduct experiments in cyclohexane, as George Bakale did earlier.

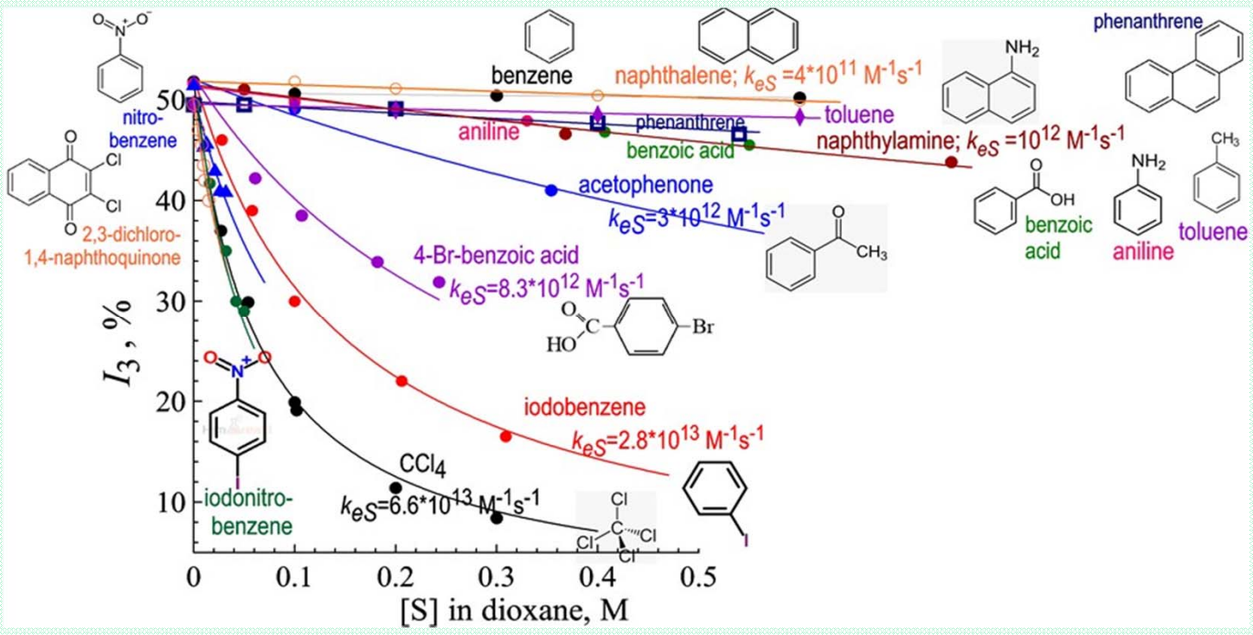




But we have to replace cyclohexane with dioxane because:

1. cyclohexane is a rather volatile liquid and its solutions may change their composition during measurements, because we have to continuously blow it with argon to remove dissolved oxygen;
2. the Ps yield in dioxane is high enough (52%), which is convenient for measurements.

Inhibition of the Ps formation in dioxane solutions of aromatic/phenolic compounds



From the obtained experimental data it follows that:

1) Ps strong inhibitors are strong carcinogens;

2) Ps strong inhibitors are strong Ps quenchers;

3) the nitrogroup (NO_2) very efficiently capture track e^-. The aminogroup -NH_2, carboxylic -COOH and methyl-CH_3 group and also benzene ring are less effective track electron scavengers. Halogens (electronegative ions) may trap e+.

Conclusions:

1) The positron spectroscopy may be used for fast detection of carcinogenic hazardous compounds. Its use turns out to be much easier, cheaper and compact then application of the pulse radiolysis technique;

2) Our method (like the Bakale one) is based on correlation between the carcinogenicity of the testing substance and its e- trapping rate constant. It is a consequence of the Millers' observation that (almost all) carcinogens are strong electrophiles. This correlation is confirmed by our present measurements;

3) There is an assertion that that non-polar solvents better simulate the intracellular milieu (since there are many organic compounds within a cell), and water therein is "structured", which reduces its solvation and dielectric properties. That's partly why G. Bakale conducted his experiments in cyclohexane. We are choosing dioxane to reduce volatility of the studied solutions, but keeping large Ps yield.