DECONTAMINATION OF DRUG VEGETATIVE RAW MATERIAL BY RELATIVISTIC ELECTRON BEAM

A.G. Gorbanyuk, I.L. Dikiy*, A.M. Egorov, N.M. Zemliansky,*
V.A. Kiselev, A.F. Linnik, V.I. Mirny, I.N. Onishchenko, V.V. Uskov
Institute of plasma electronics and new methods of acceleration NSC KIPT,
**National Pharmaceutical Academy of Ukraine, Kharkov*

The new technology of decontamination of drug vegetative raw material and medical products is proposed. Advantages of use of relativistic beams in a range of electron energies from 0.5 MeV to 5 MeV for these purposes are shown in comparison with X-radiation of energy from 80 keV to 1 MeV.

PACS: 29.27.-a

Biologically active materials now are widely used in food and pharmaceutical industry. Earlier the majority of such substances were produced by synthetic way. However growth of side reactions and weak decomposition of these substances in a human body, resulting in their accumulation in natural waters has induced to allocation of such substances from vegetative raw material. Therefore, in the last decade the interest of the largest pharmaceutical corporations to search valuable natural compounds for making on their basis components for food has increased. In this connection a special significance determination of the possibility to use the new physical methods of processing vegetative material for making resource saving technologies of phyto-preparation production, and also providing of microbe cleanness, both vegetative raw material, and ready medical products.

We had jointly performed series of experiments with the purpose to elaborate a new technology of production of medical products with a sufficient degree of microbe cleanness by means of radiation treatment of vegetative raw material by a relativistic electron beam (REB). In experiments the solution of the following problems was supposed:

- To determine the optimum radiation dose being not influential in a chemical compound of irradiated substance but sufficient for obtaining microbe cleanness of a specimen;
- To carry out the comparison of decontamination efficiency by the use of the ionizing radiation of various types (relativistic electron beam and X-radiation);
- To determine the dependence of sterilization efficiency on the electron energy and X-radiation.
- To ascertain the dependence of decontamination efficiency on the path length of electrons in treated substance.

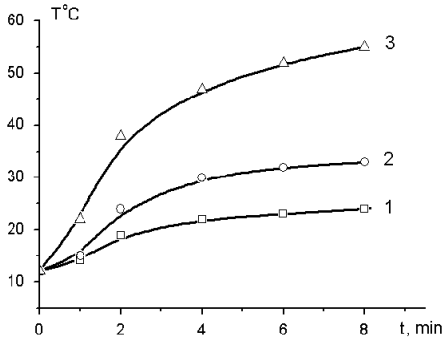
For irradiation of drug raw material the electron linear accelerator "Almaz-2" in the NSC KIPT with the following parameters of electron beam was used:
energy of 3 MeV, pulsed current of 1 A, pulse duration of 2 μsec, repetition frequency of 3 Hz. The electron beam goes out in an atmosphere through a titanic foil of a width 50 microns. Electron beam diameter near the foil is ≈1 cm. Explored specimens were placed apart = 20 cm from the output foil where the electron beam diameter was equal ≈ 8 cm. The integrated power radiation dose at such a distance was 10^4 Rad/s.

Treatment of specimens by X-radiation was carried out at the installations "Almaz-2" and "Gorizont". In the first case the stainless steel plate was placed on the way of REB in which the electron beam was completely stopped. Intensity of X-radiation behind the plate consists 60 kR per hour, radiation had a wide energy spectrum with maximum near $E_{h\nu}$ = 1 MeV. In the second case the intensity of X-radiation was 10 kR per hour with a maximum energy 80 keV. As a result, the performed control of the microbe contamination of samples has shown that the samples, processed by X-radiation, have continuous growth of bacteria on NA and continuous growth of funguses on medium Saburo. Samples were irradiated with doses in the range from 500 R up to 60 kR. The maximum irradiation time was 1 hour at the energy $E_{h\nu}$= 1 MeV and 6 hours at the energy $E_{h\nu}$ = 80 κeV. At irradiation of samples by relativistic electrons, with radiation dose from 1.2 MRad and higher, growth of microorganisms is not detected. At a dose of 0.6 MRad the growth of bacteria (500 CFU in 1 g) and growth of funguses (500 CFU in 1 g) is observed. The content of funguses exceeds the admissible norms. The minimal irradiation time by electrons after which the growth of microorganisms and funguses is not observed is 2...3 min (Table). In this table: NG – no growth; CG – continuous growth.

The name of a sample (capsule)	CFU in 1g		Presence of bacteria family
	Bacteria	Funguses	Entero-bacteriaceal, Paerudinosa, Staphylococcus
1e – 600 kRad	500	500	NG
2e – 1200 kRad	NG	NG	– // –
3e – 2400 kRad	– // –	– // –	– // –
4e – 4800 kRad	– // –	– // –	– // –
5e – 6000 kRad	– // –	– // –	– // –
6e – 8000 kRad	– // –	– // –	– // –
1p – 500 R	CG	CG	CG
2p – 1 kR	– // –	– // –	– // –
3p – 5 kR	– // –	– // –	– // –
4p – 10 kR	– // –	– // –	– // –
5p – 30 kR	– // –	– // –	– // –
6p – 60 kR	– // –	– // –	– // –

Thus by a degree microbe contamination the samples irradiated by relativistic electrons with radiation dose from 1.2 MRad and higher correspond to requirements SP-XI (the State Pharmacopoeia of Ukraine).

Samples irradiated with relativistic electrons at radiation doses of lower 1.2 MRad and X-radiation with doses up to 60 kR do not reduce to sufficient decontamination. It has been found that at the equal doses of relativistic electrons radiation the decontamination degree was practically the same at change of electrons energy from 0.5 up to 2 MeV. Radiation damages of substance did not exceed 0.01%. Necessary requirement for irradiation of medical products is the right temperature regime because at temperature higher 50°C the albumen decomposition takes place. At repetition rate 3 Hz the temperature of irradiated medicinal raw material did not exceed 35°C, at accommodation of a capsule apart 5 cm from an output foil and 25°C at distance 15 cm (at an ambient temperature 14°C). As, the repetition rate up to 5 Hz increased, the irradiated substance was heated up to temperature higher than 50°C.



Dependence of temperature of irradiated medicinal raw material on processing time:
1 *– l =15 cm (τ =3 s^{-1}),* ***2*** *– l = 5 cm (τ = 3 s^{-1}),*
3 *– l = 15 cm (τ = 5 s^{-1})*

Experiments on comparison of decontamination degree with the help the REB irradiation are carried out at location of a capsule with irradiated medicinal raw material in air and in vacuum at equal radiation dose. If the radiation dose is equal 1 MRad decontamination efficiency in air is twice higher than in vacuum. The total number of microorganisms in 1 g decontaminated in air and in vacuum was 50 and 100 accordingly for funguses – 16 and 30 accordingly. Up to now the reason of this difference is not revealed however from previous research carried out before during REB transportation in an atmosphere. It is known, that the electron beam produces plasma and under particular conditions effectively interacts with it. Thus the HF-radiation, the soft X-radiation and the accelerated plasma electrons can influence on the irradiated substance [1]. However, on our opinion, the increase of a decontamination degree in air is caused by joint action on the irradiated substance both of electron beam and ozone [2] formed by a REB in air, the value of in our measurements is 0.1 mg/m^3. Besides, as it is noted in [3] in the oxygen plasma (or in the plasma obtained in an atmosphere) electronic-excited atoms and molecules of oxygen and oscillating-activated molecules of oxygen play one of the main roles during sterilization. Presence of such molecules in plasma produced by REB in atmosphere is shown in [1]. It should be noted that the efficiency of plasma sterilization considerably falls down in the presence of capsular pathogenic microorganisms and decreases up to 10^7 spores/cm^2 as the spore density at the surface of a plant under irradiation is increasing [3]. Application of REB, on our point of view leads to destruction of capsules and bundle of spores that essentially enhances the efficiency of sterilization. Thus it is possible to make the following conclusions of the performed experiments:

- The optimum radiation dose of REB at which the degree microbe contamination satisfies the requirements of SP-XI with the minimal radiation damages is in the limits 1.2...1.5 MRad over the range energies of electrons 0.5...3 MeV.
- For irradiation of medical products with the purpose of their decontamination it is more preferable to use the REB as the result is attained for shorter time (2...3 min) while X-radiation during 1...6 hours did not give positive results.
- Efficiency decontamination is constant over all the path length of electrons in irradiated substance.
- On our judgment, it is the best way to use REB with energy from 2 MeV up to 5 MeV as the decrease of energy raises difficulties on electron beam injection into atmosphere, and shortening of the path length of electrons in substance at lower energies leads to reduction of irradiated substance volume. On the other hand, the increase of the energy above 5 MeV can result in appearance of induced and residual radiation in the specimen to be treated.

REFERENCES

1. V.A. Kiselev, A.K. Berezin, Ya.B. Fajnberg et al. // *JETP Letters.* 1989, v.29, No.12, p.762-769.
2. E.M. Babich, V.S. Gladkov, E.A. Kornilov et al. // *Ecology and resource economy.* 2001, No.6, p.40-43.
3. I.A. Soloshenko et al. // *Plasma physics*. 2000, v.26, No.9, p.845-853.

ДЕКОНТОМИНАЦИЯ РАСТИТЕЛЬНОГО ЛЕКАРСТВЕННОГО СЫРЬЯ РЕЛЯТИВИСТСКИМ ЭЛЕКТРОННЫМ ПУЧКОМ

А.М. Егоров, Н.М. Землянский, В.А. Киселев, А.Ф. Линник, В.И. Мирный, И.Н. Онищенко, В.В. Усков, А.Г. Горбанюк, И.Л. Дикий

Предложена новая технология деконтаминации растительного медицинского сырья и лечебных препаратов. Показаны преимущества использования для этой цели релятивистских электронных пучков с энергией от 0,5 до 5 МэВ по сравнению с рентгеновским излучением с энергией от 80 кэВ до 1 МэВ.

ДЕКОНТАМІНАЦІЯ РОСЛИННОЇ ЛІКАРСЬКОЇ СИРОВИНИ РЕЛЯТИВІСТСЬКИМ ЕЛЕКТРОННИМ ПУЧКОМ

О.М. Єгоров, М.М. Землянський, В.А. Кисельов, А.Ф. Линник, В.І. Мирний, І.М. Онищенко, В.В. Усков, А.Г. Горбанюк, І.Л. Дикий

Запропонована нова технологія деконтамінації рослинної лікарської сировини та лікарських препаратів. Показані переваги використання з цією метою релятивістських електронних пучків з енергією від 0,5 до 5 МеВ порівняно з рентгенівським випромінюванням з енергією від 80 кеВ до 1 МеВ.