REVIEW ON THE MECHANISMS OF NON-THERMAL BIOEFFECTS OF ELECTROMAGNETIC WAVES AND THE EXPERIMENTAL STUDY ON BIOEFFECTS OF TRANSIENT ELECTROMAGNETIC FIELDS ON CELLS AND ITS APPLICATIONS*

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Abstract: Many hot problems of non-thermal effects of electromagnetic waves, such as the effects on human beings of low frequency electric fields and the mechanism of the interaction between biology body and low-intensity electromagnetic fields, were discussed in this paper. Moreover, the experimental studies of transient electromagnetic fields leading to cell membrane deformation were studied and its possible applications were presented.
Key words: non-thermal bioeffects, transient electromagnetic pulses, electroporation

I. Introduction

In the last 100 years, the bioeffects of continuous electromagnetic waves had been studied very well, and some important steps were performed. The studies covered stages from thermal bioeffects to non-thermal bioeffects, from animal to cells and biological macromolecular, from bioeffects to clinical applications[1-3]. However, there were few studies on transient electromagnetic fields, which were several or a series of electromagnetic pulses with high amplitude and very short rising time. The mechanism and features of non-thermal bioeffects will be discussed in this paper, especially the phenomena of low-intensity transient electromagnetic pulses leading to pores on cell membrane and its possible applications will also be presented.

II. Hot problems on non-thermal bioeffects

The features of non-thermal bioeffects are: A) Nonlinear process—weak electromagnetic fields can lead to obvious bioeffects, and the relation between bioeffects and the intensity of the electromagnetic fields is nonlinear. B) Frequency window and power window—only at some frequency and/or some power density the electromagnetic fields can lead to obvious bioeffects, which can be proved by the calcium ion flux in brain tissue affected by electromagnetic fields. C) Energy source—the energy from biological body is larger than that from the electromagnetic fields in the bioeffects. There is an avalanche energy respond from the biological body. The energy from electromagnetic fields induced the process, and the main energy comes from the biological body itself.

In the early study on mechanism of non-thermal bioeffects, explains to these are as followings: A) Theory of coherent electric oscillator presented by Frohlich. It is believed that there is coherence and synergism in biological body. When the frequency of the electromagnetic field is very near to the coherent frequency of the biological body, it can either destroy or build the coherence. Then the activity of biological body will be affected. B) Theory of ion cyclotron resonance. The electromagnetic fields can alter the polar moment of the ion channel. With the ion's cyclotron movement inside the ion channel, it can affect the process of ions crossing the membrane. C) Theory of ion permeability to the membrane. It means that the electromagnetic fields can affect the permeability of the membrane. Meanwhile, the electromagnetic fields can induce an additional transmembrane potential, which can affect the permeability of membrane and then lead to bioeffects. D) Effects of free radical. Electromagnetic fields can affect the composition rate of paramagnetic free radicals. Then the life period of the free radicals will be changed, and it can alter the transient concentration of the free radicals, which will lead to bioeffects. Besides these theories, there are some other theories to explain the non-thermal bioeffects, such as the theory of electromagnetic interference factor and the theory of pores on membrane due to electromagnetic pulses, and so on.

In resent years, there are some hot problems on the interaction between electromagnetic fields and biological body[4]. Here is a brief list: A) The dangers of extremely low-frequency fields (ELF) to human beings (especially for those who are living near to the high-voltage electric power line). Many researches found that there was a certain relation between power frequency exposure and cancer incidence rate. It was shown that leukaemia incidence rate of the children living near the high-voltage power line was higher than normal from the investigation data of WHO and ICNIRP. It was believed that the leukaemia incidence rate of the children living near to the high voltage power line was 1.5 times of the normal children. NIEHS concluded that ELF was a possible carcinogen for human being. B) The mechanism of the interaction between low-intensity field and biological body. Why does the weak electromagnetic fields lead to strong biological respond? One common opinion is that the chemical transfer system in the cell communication may be one of the key objects of the outside electromagnetic fields. Electromagnetic fields act on the membrane as a information factor, then activate an under-controlled metabolism and a cascade reaction of the enzyme system by the cell signal transduction. It may lead to the change of gene duplication and transformation. Moreover it will lead to the respond of cell hyperplasia and/or differentiation. Further studies are needed in this field. C) How does the electromagnetic fields affect the melatonin? Up to now, it is known that the periodic change of the melatonin concentration in the serum is the main hormone to keep the biological clock, and one of the main reasons of the melatonin change is the activity of periodic light activity. It is proved by experiments that magnetic fields can reduce the melatonin concentration in the mature hamster serum. It could be induced that magnetic field's affect is at the same way with the sunlight. D) Pollution of the mobile communication. Many reports show that there is none directly relation between

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the mobile phone use and cancer incidence rate. So it is still under discussion, and further study is needed[5].

III. Effects of low-intensity transient electromagnetic pulses to cells

In recent twenty years, since the rapid development of electromagnetic pulses (EMP) techniques and its applications, the bioeffects of EMP have attracted more attentions. Compared to continuous wave, EMP is a broadband signal, which can cover the frequency range from zero Hertz to 10^9 Hertz. So the generator, transmission, irradiation and scattering of EMP is much different from continuous wave. In the experimental system, a broadband equipment, such as a BTEM Cell, has to be used to make the pulses transmitted without form distortion. Moreover, some concepts usually used in continuous wave, such as average power density, have no means for EMP, since for periodic pulses when the interval between pulses is far great than the width of the pulse the average power density is near to zero. In this case, the amplitude, rising time and pulse width are the key electromagnetic parameters.

In some researches, it is found that EMPs can lead affect the cells of human beings. Since cell is the fundamental unit of both the structure and the function of biological body, most of the researches are in this biological level. The further study shows that the original point may be on the membrane. Some EMPs with the intensity of several kV/m can lead to pores on membrane, which is similar to electroporation. Before the membrane electric breakdown value has reached, some voltage sensitive protein ion channel will open to form random openings on the membrane. Then stronger current will flow the openings and the osmotic pressure will be much different. Finally, it will lead to a pore on the membrane.

Based our researches in this field, a brief introduction to the possible application in biomedical engineering is presented.

First, the experimental study of low-intensity EMP lead to the increase of anticancer drugs cytotoxicity. Periodic rectangle pulses with the amplitude of 187V and pulse width of 50ns were used at a 300Hz repeat frequency. Chick blood was put in the center of BTEM Cell where the electric intensity is near to 2000V/cm. We found that the rate of pores on membranes was greater than 2% and diameter of the pores is from 20nm to 500nm, as shown in the following figure.

Cancer cells Re-07, Lu-06 and Col-05 were mixed with C7 (fat-soluble) and CPT (water-soluble) separately and put into BTEM Cell to accept irradiation for 50 or 100 min. SRB method was used to measure the OD value, which can reflect the number of cancer cells. If there are pores on the membranes, more anticancer drugs will enter the cancer cells and the cytotoxicity of anticancer drugs will be increased. Experimental results showed that OD values of C7 group drop 52%-85%, which mean EMP irradiation increased the cytotoxicity of C7 anticancer drug. But for the CPT group, there was no obvious change. The possible reason is that C7 is fat-soluble and smaller than CPT.

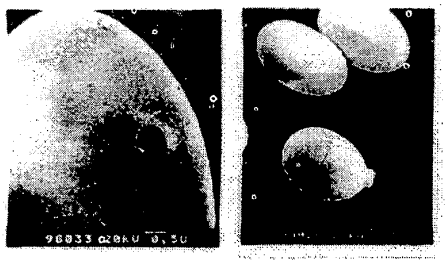

Figure: Photos of pores on cell membrane

Second, rabbit blood was used to perform the experiments. The results showed that low-intensity EMPs could lead to stronger effects than that of chick red blood cells. The rate of pores on membrane was near to 60%, and the diameter of pores could reach 0.6 m-1.3 m. These phenomena may have many possible applications.

Third, the gene transfection due to low-intensity EMP is studied. Yeast 54.s.Cerevisiae DC5 and plasma YRP12-54 were used in the experiments. After irradiation of EMP with 2000V/m intensity for 20 min, it was successfully found that plasma had entered the yeast. So this experiment proved that low-intensity EMP could lead the out genes to enter the cell and insert into the gene group of the cell. This method for gene transfection has a very bright future in the applications of biomedical engineering.

The study on the applications of transient EMP in biomedical engineering is in the initial step. Following the development of techniques, there must be some new achievements in this field.

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