

Self review

Regulatory effects of terahertz waves

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Abstract: There are modern data about biological effects of terahertz (THz) waves in this article. Items of interaction of THz waves with bio objects of different organization level. A complex of the data indicates that the realization of a THz wave effect in biosystems is possible at molecular, cellular, tissular, organ and system levels of regulation. There are data about changes in nervous and humoral regulation of an organism and metabolic effects of THz waves.

Keywords: terahertz waves, regulation

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Radionics progress and its adoption to all spheres of science, techniques and everyday life is an essential part of civilization [1-3]. Among an amount of environmental factors causing significant changes in a functional condition of biological systems of different organization levels, the main role belongs to electromagnetic irradiations (EMI) [4, 5].

Terahertz (THz) therapy is a relatively new, but rather advanced physiotherapeutic method of treatment [6-8]. Biological effects of THz radiation are registered at an irradiation power flux density significantly lower than 10 mW/cm². At such a low intensity an integrated heating of irradiated objects in the experiment is no more than 0.1°C. That is why THz electromagnetic radiation is classified as informational, nonthermal exposures [9].

A feature of terahertz waves to expose bioobjects is characterized by locating in this band of its fundamental frequencies of vibrational-rotational transitions of water and biological molecules (prime and composite), as well as big polymers (polypeptides, proteins) [10]. It is known that molecular emission and absorption spectra (MEAS) of many bioactive substances (nitrogen oxide – NO, carbon oxide – CO, molecular oxygen and its active forms, etc.) are in THz band [11, 12]. Besides, in submillimeter part of THz band, according to theoretical calculations and measurements, there are fundamental frequencies of membrane, intracellular machinery and cells vibrations. This may cause resonance effects at a coincidence with frequencies of external electromagnetic irradiation [13].

Biological effects of terahertz waves at a molecular level

A significant effect of this irradiation on biopolymers condition had been experimentally proved. During the THz irradiation of

albumin protein samples there had been revealed conformational transitions of these macromolecules. These transitions had been registered by different spectroscopic methods, which let fix changes in correlation fractions of condensed and folded structures, and changes in optical albumin density in absorption area of peptid and disulfide bonds [14-17]. This indicates that THz irradiation induces conformational change in albumin molecules caused by the change in its bonding property. This fact is confirmed by the study of persistent THz irradiation influence of 3.68 THz frequency on bonding albumin with progesterone, which is performed by hydrophobic interaction of bonding centers with rests of triptophane, tyrosine, arginine and lysine. It had been showed that albumin bonding property, irradiated by THz waves, increases [14, 18].

Today a dynamics of change in the level of antioxidant enzymes: superoxide dismutase of aurococcus, catalase, peroxidase, collibacillus and blue pus organism under the influence of THz electromagnetic waves of MEAS of atmospheric oxygen (129 GHz) and MEAS of nitrogen oxide (150.176–150.664 GHz). It had been revealed an increase of antioxidant enzymes potency of radiated organisms races, the most evident at 45-minute exposition of THz waves of 129 GHz, and at 45- and 60-minute expositions of THz waves of 150.176–150.664 GHz [19-21]. It had been also fixed that THz waves of 150.176–150.664 GHz cause a recovery of normal superoxide dismutase and catalase potency of erythrocytes in white rats under the acute immobilization stress condition [22]. Change in intermolecular protein interactions under the THz waves irradiation had been demonstrated by the example of change in stability of antigen-antibody complex under the electromagnetic waves irradiation of 100 GHz [23]. So one of the significant molecular mechanisms of THz waves is a change in enzymes and enzymatic systems in cells.

Subcellular level of effects realization of THz waves

THz waves influence cell membranes. So in the experiments of the study of THz waves effect on osmolar resistance of erythrocytes in mice, and it had been showed that electromagnetic irradiation of 3.68 THz increases a low cell membrane resistance [24]. It had been found out an influence of THz (submillimeter) irradiation on processes of transmembrane traffic in neurons. Set of experiments with the use of a coloring material which does not penetrate through intact membranes (Trypan Blue), and reveals living cell, and electrophysiological analyze showed that THz irradiation creates conditions for penetrating of those substances into living cells, which do not usually penetrate [25]. Besides, it had been established that penetrance of phospholipid liposomes increases significantly after 130 GHz irradiation with density 10-17 mW/cm² [26].

Thus, mechanisms of molecular and subcellular levels take part in effects realization of THz waves. Change in enzymatic systems activity and cell membrane properties are typical to THz irradiation as well as to waves of other bands.

Cellular level of effects realization of THz waves

There is an amount of descriptions of the cellular effects of THz irradiation in medical literature. So it had been established that THz irradiation of 3.68 THz intensifies spontaneous and mainly induced mitoses of human lymphocytes. It had been displayed that THz waves have differently directed effect in lymphocytes population and the cell reaction on the irradiation depends on its functional condition [24]. Moreover, THz waves influence also intercellular interactions. So, it had been fixed that thrombocytes incubation in the patients with unstable angina with blood platelets, irradiated by THz waves of 150.176–150.664 GHz of NO, causes a decrease of activity [27].

Besides, it had been displayed that incubation in the system irradiated by the given waves and non-irradiated blood of the patients with unstable angina causes a reliable increase of a blood viscosity [28]. We had fixed that mitotic activity of irradiated lymphocytes (3.68 THz) is higher in the presence of irradiated monocytes then at a contact with non-irradiated monocytes [15]. Effect of THz waves on monocyte-macrophage system is realized not only by the effect on regulatory monocyte function, but also by macrophage phagocytic activity. We had demonstrated that THz irradiation of 150.176–150.664 GHz of NO exposure on peritoneal macrophage increases extremely their phagocytic activity. This is evident as from an increase of the percent of cells taking part in a phagocytosis process (phagocytic index) as from an increase of bacterial cells number occupied by one macrophage (phagocytic number) [29].

Erythrocytes, causing blood viscosity properties, are sensitive evidently to THz irradiation at in vitro conditions. In the study of N.V. Mamontova [30] there had been established the fact of a normalization of defected blood viscosity properties, erythrocytes aggregation and deformability in the patients with unstable angina under the natural electromagnetic field of EMI on 240 GHz (the most evident at 15-minute irradiation mode). There had also been demonstrated a statistically valid normalization of blood viscosity properties, erythrocytes aggregation and deformability in the patients with unstable angina in crossed magnetic and electric fields under 240 GHz EMI (the most evident at 15-minute irradiation mode) [30]. The authors had also denoted that 30 minutes is an interaction time of EMI with terahertz frequencies (THF) (240 GHz) normalizing effect influences blood viscosity

properties, erythrocytes aggregation and deformability in the patients with unstable angina at in vitro conditions [30].

A.P. Krenitckiy, A.V. Maiborodin, V.D. Tupikin et al. [31] had showed normalization of thrombocyte functional activity in the patients with unstable angina under EMI of NO THF (240 GHz), which was accompanied by statistically valid decrease of a maximal size of appearing thrombocytic aggregates, maximal speed of the most thrombocytic aggregates appearing, maximal aggregation degree [31] (at in vitro conditions).

We [32] had also displayed that at EMI of NO THF (400 GHz) enriched by thrombocytes of the patients with unstable angina plasma (at in vitro conditions), there was a significant decrease of blood platelets aggregability, which had been accompanied by statistically valid decrease of a maximal size of appearing thrombocytic aggregates, maximal speed and aggregation degree.

It had been revealed a significant effect of THz waves on neurons at in vitro conditions. In a pond snail (*Lymnaea stagnalis*) isolated neurons the most evident effect of THz irradiation of 0.7, 2.49 and 3.69 THz was on cells growth, their adhesion, membrane morphology change and intercellular structures, and the value of membrane resting potential. As a result, we can see that THz waves significantly influence morpho-functional neurons condition, this predetermines a realization of effects in nervous system [33-35].

Thus, the given data indicate that the mechanism of THz waves can be realized at a cellular level. Change in regulatory mechanisms of molecular, subcellular and cellular levels will lead to realization of influence on functional condition of tissues, organs and a whole organism.

THz waves effect on nervous and humoral regulating functions of an organism

Studies in THz waves influence on cells, tissues, organs and organ systems generate a significant interest (at in vitro conditions). First, it should be noted changes in nervous and humoral regulating functions under THz irradiation. So, it had been denoted that THz waves can influence the central nervous system and the higher nervous activity of animals. It had been indicated that a high power THz irradiation (60-minutes) of MEAS of NO (150.176–150.664 GHz) in male rats under the acute immobilization stress, leads to a depression of a motion activity. This was evident from a statistically valid increase of a total time that animals had spent in Small Labyrinth, and a total time of animals' washing process [36,37].

Experimental studying display that THz waves of different frequencies can cause various changes in behavioral reactions. It had been established that male rats which had got a 5-day long low-intensity waves of 167 GHz, kept normal searching reactions, curiosity, active positive communication, as irradiated animals of the same length and power of 144 GHz had an anxious behavior, reduced appetite and sleep time, displayed aggression [38].

With the help of experiments on laboratory mice it had been fixed that 3.68 THz irradiation causes reaction of avoiding, displacement of a motion activity and state anxiety which do not disappear on the next day of irradiation [39].

The results given below display that THz irradiation have a significant effect on behavioral reactions, and, as a result, on the central nervous system and the higher nervous activity of animals. A variety of effects of THz irradiation depending of a frequency comes under notice.

There are data about THz irradiation effect on humoral regulating function of an organism. There had been showed that at a 5-day long THz irradiation with NO frequencies (150.176–150.664 GHz) (30 minute), a total normalization of defected functional activity of thyroid body was denoted in male rats. At the same time the concentration of free and bonded thyroxin and triiodothyronine fractions, thyroglobulin concentration, proportion T_3/T_4 and thyreotrophin had been normalized and statistically valid had not differ from the control group. The presented indices indicate that at the given irradiation there is a total normalization of thyroid body activity [40, 41].

It had been established that THz waves have different effects on adrenal body condition in rats under stress depending on a frequency. Irradiating of rats with a 5-day 15-minute exposition of 167 GHz after 3-hour immobilization prevents hypertrophia of adrenal body in stress and typical histological change developing. The same exposition but of 144 GHz increases morphological changes in adrenal body in stress [42]. It had been showed that THz irradiation of MEAS of 129 GHz atmospheric oxygen stimulates a decrease of corticosterone concentration in male rats under acute and prolonged stress. Single-shot persistent 15-minute irradiation of THz band of the given frequency (on the background of acute immobilization stress) totally normalizes defected corticosterone concentration in experimental animals. The most effective irradiation time mode at the prolonged stress is a 5-day 30-minute exposition of 150.176–150.664 GHz of NO can prevent corticotrophin expulsion in white rats at immobilization stress [45].

Thus, the effect of THz waves can change as nervous as humoral regulating mechanism in an organism.

Metabolic effects of THz waves

Experimental research displays that THz waves have a variety of metabolic effects. It had been demonstrated a possibility of metabolic status correction (carbon, lipid and protein balance) with the use of EMI of 150.176–150.664 GHz of NO of male rats under the acute immobilization stress. A 5-day 15-minute exposition of the same frequency can effectively reduce a high triglycerids concentration in animals' blood. Time mode increasing of exposition up to 30 minutes normalizes glucose and triglycerids level in blood.

A 30-minute exposition of electromagnetic waves corrects glucose, creatinine and urea in blood serum in rats under prolonged immobilization stress [46].

There had also been fixed normalization of protein metabolism in an organism. A 30-minute exposition of electromagnetic waves 150.176–150.664 GHz of NO rats under acute stress causes normalization a protein concentration in blood plasma, recovery of a proportion of protein fractions: albumin level increases, percentage concentration of protein of globulin fraction significantly decreases. There is a decrease of high concentrations of α_1 -, α_2 - and β - globulins comparing with non-irradiated animals under acute stress [47].

Besides, there had been fixed a normalizing effect of THz waves 150.176–150.664 GHz (NO) on activity of plasma enzymes in rats under prolonged immobilization stress. So at this irradiation there is a normalization of changed transaminase, glutathione-S-transferase, lactic dehydrogenase activity and ceruloplasmin in blood plasma [46, 47].

Lipid peroxidation (LPO) has a significant value among metabolic effects of THz irradiation. It is known that defects in LPO

processes are one of common pathogenesis mechanisms of variable diseases, cardiovascular failures as well [48]. It had been indicated that THz waves 150.176–150.664 GHz of NO cause toxic lipid peroxidation intermediate products (lipid hydroperoxides, malondialdehyde) in blood serum and erythrocytes, and cytolysis and autointoxication markers (molecules of an average mass) in rats' blood under acute immobilization stress. A decrease of molecules of an average mass level in a blood serum under acute immobilization stress at the THz waves exposure indicates a decrease of an autointoxication degree and reduce of cytolysis syndrome [49].

An oxidoreduction balance in an organism is tightly connected with a blood gas recovery. It had been fixed that at the THz waves 150.176–150.664 GHz of NO there was an increase of a partial pressure of arterial oxygen in male rats under acute and prolonged immobilization stress [50, 51].

Thus, electromagnetic waves of THz band influence significantly the mechanisms of nervous and endocrine control and metabolic status in a whole organism.

THz waves effects on different organs and organ systems condition

Over the last years there have been new data appeared about an effect of THz waves of different frequencies on a structure of some tissues, organs and systems. In particular it had been indicated an effect of THz waves of 150.176–150.664 GHz on cartilaginous tissues condition in white rats under acute and prolonged immobilization stress. In experimental animals under THz waves of 150.176–150.664 GHz on the background of acute and prolonged immobilization stress, there was a decrease of dilatation and color variations of collagen fibers in cartilaginous tissues, normalization of its homogeneity, seldom episodes of vacuolization and chondrocyte karyopyknosis [52].

It had been revealed an effect of THz waves of 167 GHz and 144 GHz on structure-functional change in renal of male rats under stress condition. The results of the experiment indicate a useful restructure post-stress effect of EMI of 167 GHz on a morpho-functional renal condition in male rats. At the same time EMI of 144 GHz does not influence a functional morphology of cortical and periencephalic nephron in male rats under stress [53].

Effects of THz waves on a blood system are to pay particular attention. The experimental results of O.N. Antipova et al. [54-58] display that the 15- and 30-minute exposition of THz waves of 150.176–150.664 GHz (NO) in animals under acute immobilization stress causes a total normalization of a blood viscosity under different rates-of-shear. The results analyze of blood rheological properties in animals under prolonged stress showed the normalization of a blood viscosity properties under low and high rates-of-shear.

It had been established that a normalization of an intravascular microcirculation component at THz waves of 150.176–150.664 GHz in male rats under acute and prolonged immobilization stress is correlated with a decrease of high erythrocytes aggregation and caused by recovery of their receptor apparatus activity. Under the given exposure there is a normalization of β -D-galactose in a carbohydrate component and a recovery of a glycoprotein erythrocyte receptors in male rats under acute and prolonged immobilization stress [59, 60].

O.I. Pomoshnikova [61] had found out that THz waves of 150.176–150.664 GHz partially or totally normalize intravascular

microcirculation component after stress by recovery of quantitative and qualitative erythrocyte components depending on a regime and time mode. The author considers that 15-minute time mode of irradiation is the most effective in normalization of quantitative and qualitative erythrocyte components. A daily 30-minute irradiation on animals under prolonged immobilization stress normalizes an average hemoglobin concentration in erythrocytes and their average size and aggregability [59].

It had been showed that EMI of THz band of MEAS of 150.176–150.664 GHz of NO can normalize thrombocyte functional activity in white male rats under acute immobilization stress [62, 63]. Under the given exposure there is a normalization of thrombocyte receptor apparatus activity, this stimulates a recovery of intravascular microcirculation component in male rats under acute immobilization stress [64, 65].

S.V. Sukhova et al. [66] had studied EMI of THz of 129.0 GHz atmospheric oxygen effect on a thrombocyte functional activity in male rats under immobilization stress. It had been indicated that in a 5-minute 129.0 GHz THz irradiation there was a normalization of thrombocyte functional activity in male rats on the background of immobilization stress.

The authors consider that there are mediators of EMI of THz band in cells and biological fluids are active forms of oxygen (AFO) which are, probably, formed enzymatically by change in protein molecules hydration and increase of cyclooxygenase and xanthine oxidase activity [67]. AFO stimulates a soluble guanylate cyclase by Ca^{2+} , this causes a high concentration of cyclic guanosine monophosphate (cGMP) in endothelial vessels cells and an increase of NO-synthase activity which increases NO producing [67]. This can be one of mechanisms of antiaggregate and antistress effects of THz waves of MEAS of 129.0 GHz atmospheric oxygen [66].

Today we have information about a significant effect of THz waves on clotting and fibrinolysis. So it had been showed that under the persistent exposure of MEAS of 150.176–150.664 GHz (on the background of acute immobilization stress) there was a normalization of pro-coagulant, anticoagulant and fibrinolytic activity in blood of rats. It had been established that the most effective time mode was a 30-minute irradiation. It was revealed that a proximate irradiation of animals before the stressor action in a persistent mode prevents the developing of defects in different phases of clotting and fibrinolysis. A divided irradiation mode of animals causes a total normalization of coagulant component in a hemostasis system and fibrinolysis – at a 15-minute THz irradiation of MEAS of 150.176–150.664 GHz of NO. It means that an efficiency of THz waves on a hemostasis system at a whole organism conditions is determined not only by an exposition, but an irradiation regime [68-70].

Besides, it had been established that THz waves of MEAS of 150.176–150.664 GHz corrects effectively not only acute, but also prolonged defects in a hemostasis system. A daily proximate 30-minute irradiation of animals at a chronic immobilization stress condition totally prevents failures in clotting systems and fibrinolysis [71-73]. THz waves of MEAS of 129.0 GHz atmospheric oxygen can stimulate a normalization of clotting, anticoagulant and fibrinolytic activity in blood of rats under immobilization stress. The effect of THz waves of this band, as well as the NO band, on parameters of a clotting component of hemostasis system (activated partial thromboplastin time, prothrombin time, international normalized ratio, fibrinogen concentration, thrombin

time value, factor XII activity in blood plasma depends on an exposition time). It had been fixed that a 5-minute exposition does not cause change in defected parameters of clotting, a 15-minute exposition leads to a partial normalization, a 30-minute exposition leads to a total normalization of clotting activity in rats' blood at experimental stress-reaction [74]. Analogical changes had been noticed by the authors during the study of fibrinolytic activity. It is showed that the most evident normalization of Hageman-kallikrein-dependent fibrinolysis, and plasminogen reserve index in white rats under acute immobilization stress, is noted at a 30-minute exposition of electromagnetic waves of MEAS of 129.0 GHz atmospheric oxygen [74].

The presented data display a significant effect of THz waves on parameters of intravascular microcirculation component: hemostasis system and blood rheology components. There had also been described several effects of THz waves on a cardiovascular system. In particular it had been showed a normalizing effect of 150.176–150.664 GHz frequency in rats (under acute immobilization stress) on parameters of hemodynamics in abdominal aorta part and femoral artery [75-77].

Besides, THz waves of NO frequency have a normalizing effect on microvasculature refusion in male rats under acute and prolonged immobilization stress [78-81]. Realization of hemodynamic effects of THz waves of 150.176–150.664 GHz of NO in male rats under acute and prolonged immobilization stress is performed by an effect on paracrine regulatory mechanisms of vascular endothelium. THz waves of the given frequencies cause an increase of NO producing by vascular endothelium, which is accompanied by a normalization of a decreased basic and induced vasodilating potency in animals under acute immobilization stress [82]. The exposition course in animals under prolonged stress causes an increase of nitrites concentration – NO stable metabolites [83] and a decrease of endothelin I concentration [84] in blood serum, leading to recovery of vasodilator substances balance – prevents endothelial dysfunction progress. Mechanism of THz waves of the given band is realized by the NO-synthase component cycle of NO. THz waves do not realize its positive effect on a hemodynamics in magistral arteries and microcirculatory vessels in rats under acute immobilization stress at the NO-synthase blockade [85, 86].

Thus, THz waves can change morpho-functional condition of tissues and organs, which influences on a functional organism state in the whole. The literature data indicate that strong regulating properties of many processes in an organism are typical to electromagnetic waves of the given band. Realization of biological effects of THz band electromagnetic waves is performed at a molecular, subcellular, cellular, organ and organismic levels.

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