RABBIT HEATING BY MICROWAVE EXPOSURE AT VARIOUS AMBIENT TEMPERATURES

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The potential ability of environmental temperature to enhance the effect of microwave radiation (7 GHz) was experimentally studied for rabbit heating after simultaneous application of both agents. The tested ambient temperatures (30 and 38℃) didn't exert a considerable influence upon rabbit heat homeostasis after the used duration of exposure (3 hours and 15 minutes, correspondingly). The synergistic interaction of microwave irradiation and ambient temperature was demonstrated for rabbit heating. Power flux density of microwave irradiation was shown to be a determinant of the synergistic interaction effectiveness. For the fixed ambient temperature (30℃), the synergism was shown to be observed only within a definite power flux density (0–100 mW·cm^{-2}), inside of which there was an optimal intensity (20 mW·cm^{-2}), which maximized the synergistic effect. Any deviation of the power flux density from the optimal value resulted in a reduction of the synergy. It is concluded that any assessment of the health or environmental risks should take into account the synergistic interaction between ambient temperature and microwave radiation.

Keywords : Microwave, Hyperthermia, Synergistic Interaction, Rabbit, Body Temperature, Thermoregulation

1. INTRODUCTION

One of the main biological effects of microwave radiation on living matter is an increase in the temperature of the irradiated object, which is directly proportional to the amount of energy absorbed. This is caused by the conversion of electromagnetic energy to thermal energy. Hence, both the intensity of the incident field and exposure duration are important parameters that determine the quantity of energy absorbed by tissue. There is an increasing interest to the problem of synergistic effects observed after combined action of various agents. Many studies have shown that numerous physical and chemical agents combined with heat can interact in a synergistic manner when the effect produced by both agents used in combination exceeds the expected results from a simple summation of the individual effects produced by heat and particular agent [1–3]. Some general rules have been revealed for the synergistic interactions of a simultaneous action of hyperthermia with ionizing radiation, ultraviolet light, ultrasound, and some chemicals [4–7]. First, for any constant rate of exposure, the synergy can be observed within a certain temperature range inside which there is a specific temperature that maximizes the resultant synergistic effect. Second, as the rate of exposure is reduced, this temperature range and the temperature providing the greatest synergistic effect decrease and *vice versa*. Third, for a constant temperature at which the irradiation occurs, the synergy can be observed within a certain range of exposure rate inside which an optimal intensity may be revealed that maximizes the synergistic effect. Fourth, as the exposure temperature is reduced, this range and the optimal intensity decrease and *vice versa*.

The widespread and increasing use of radio-frequency electromagnetic radiation (RFR) has greatly increased the possibility of exposure of both occupational and general population to RFR. With the rapid expansion of technologies causing increasing exposure to RFR, especially in mobile telecommunications, there are now challenges to the limit values of safety standards. Analysis of the literature on biologic effects of microwaves reveals several areas of established effects and mechanisms on the one hand and speculative effects and mechanisms on the other [8]. This has created a dilemma in trying to assess the real or imaginary from the actual or potential hazard to man from exposure to RFR [8] With the accumulation of hygienic, experimental and clinical data it became apparent

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that more strict assessment of occupational conditions is necessary for those working with RFR sources. Under natural conditions, microwave irradiation is often accompanied by other factors existing in the environment, such as a high ambient temperature, noise and toxic compounds. Studies of the biological effects resulting from such combined influences are important from theoretical and practical perspectives. First of all, it concerns a potentially increased health risk to the general public and occupationally exposed population. Secondly, there is a great difference in safety standard of microwave irradiation in various countries. Thirdly, these agents are explored in cancer treatment. It was found that ambient temperature had a profound effect on the thermogenic effect of microwave radiation of various animals [8–13]. In these experiments, the rectal temperatures had minimal fluctuations or increased slightly in the absence of microwave exposure at a higher ambient temperature. It means that ambient temperatures either exert a microwave sensitizing action or both these agents can interact with each other in a synergistic manner. The synergistic interaction takes place when the combined action of these agents exceeds the sum of their individual effects. It was found that an ambient temperature had a profound effect on the thermoregulatory responses of various animals [8–13] and men [14, 15] exposed to microwaves. In these experiments, these agents could interact with each other in a synergistic manner. However, none of these papers enables to demonstrate the dependence of the synergistic effect on the intensity of microwaves and to show the existence of the optimal power flux density, which maximizes the synergy. Thus, this study was designed to implement three purposes: (a) to reveal the synergistic interaction of microwave and environment temperature; (b) to demonstrate the dependence of synergistic interaction on the microwave power flux density; (c) to show the existence of the optimal microwave intensity, which provide the greatest synergistic effect.

2. MATERIALS AND METHODS

The RFR exposure system has been described [16–19]. Exposure to RFR were performed in a temperature-controlled anechoic chamber with dimensions of 6.5 (length) x 5.0 (width) x 3.5 (height) m, lined with commercial microwave absorbing material. The air temperatures in the chamber were initially adjusted to 22 ± 0.2℃, 30 ± 0.5℃, 38 ± 0.5℃. Animals used in this study were Shinella rabbits with body masses of 2.5 to 3.2 kg both males and females. The rabbits were purchased from Russian Academy of Medical Sciences nursery «Stolbovaya» at an age of 60 days. They were housed individually at an ambient temperature of 22℃, with a relative humidity of 50% under natural lighting. Rabbit chow and water were provided ad *libitum*. Animals were pre-handled and gentled for 10 days prior to exposure. The body temperature was allowed to equilibrate in the chamber for at least one hour before irradiation. Rabbits were individually exposed to continuous-wave microwaves at a frequency of 7 GHz. The irradiation was carried out in the far zone and E-orientation of body at (55 ± 5)% humidity. All experiments were performed with the animals without general anesthesia.

In this study, rectal temperature was measured in rabbits during and immediately following exposure to 7 GHz microwave radiation at an ambient temperature of 22, 30 or 38℃. Microwave irradiation at 38℃ was performed only for one power flux density (100 mW·cm^{-2}). Individually each rabbit in sitting position was confined in a Plexiglas cage. The walls of the cage were performed with holes (15 mm in diameter spaced 3 cm) and the top of the cage was covered with cellular net made of cotton fabric to enhance thermal equilibrium with the anechoic chamber. The rabbit was not able to move in the Plexiglas cage. Experiments were performed on 71 rabbits.

Rabbits were individually irradiated to the following power density: 0 (sham irradiation), 10, 15, 20, 30 and 100 mW·cm^{-2}. Power density measurements were made using P3-9 power meter (Russia). The corresponding specific absorption rates (SAR) were 0, 0.75, 1.12, 1.50, 2.25, and 7.5 W·kg-1. To calculate SAR, the amount of energy absorbed was determined by measuring the amount of heat generated in a fresh animal carcass irradiated with microwaves by use of a differential or a quasi-adiabatic calorimeter. The heating pattern should be measured before it is altered by blood flow and heat diffusion. Therefore dead animals have been used as a phantom material, eliminating the problems of physiological heat production and loss. Calorimetric techniques are usually used to measure the mean whole-body SAR. We have used a twin-well calorimeter similar to that used by McRee [20] but with some modifications. Twin-well calorimeters are instruments which measure mean whole-body SAR very accurately. The accuracy of these techniques has been estimated to be about of 5%. Because one of the purposes of this work was to compare the dependence of animal lethality on the average SAR and on the power flux density, the last value was obtained by P3-9 apparatus, the accuracy of measurement of the power flux density being only ± 30%.

A modified medical model TPE-1M thermometry unit (Russia), with a thermistor probe, which was shielded with Plexiglas and fixed in the rectum, was used to monitor colonic temperature during exposure. In this unit, the measured temperature range was enlarged up to 50℃, the accuracy was improved within to 0.05℃, and the diameter of temperature sensor was decreased to 1 mm. Special experiments have demonstrated that the presence of the thermistor probe during the irradiation did not exert influence upon the registered rectal temperature. During exposure, the colonic temperature was read within every 10 minutes or more frequent. Animals were not re-exposed to RF radiation. During irradiation animals were watched by TV. Other details were as was published previously [16–19].

3. EXPERIMENTAL RESULTS

We used ambient temperature of 30 ± 0.5℃ because of two thoughts: first of all, this temperature may exist at a working place of microwave equipments; secondly, in accordance with literature [19], it is an upper limit of relatively comfort temperature both for rabbit and slightly-dressed man. Actually, the presence of a small additional thermal loading (for example, microwave exposure with low intensity) may result in a disturbance of thermal balance of organism [19].

Fig. 1 shows the results of simultaneous action of microwave and ambient temperature on rabbit heating. Microwave irradiation was performed at 22 and 30℃ at power flux density of 0 (sham irradiation), 10 and 15 $mW\cdot cm^{-2}$ (Fig.1A) as well as at 20, 30 and 100 $mW\cdot cm^{-2}$ (Fig.1B). In both parts of this Figure the increment of rectal temperature exhibited by animals are depicted. One can see that at an ambient temperature of 22℃, the rectal temperature increment was negligible after 180 min exposure at power flux densities of 10 and 15 $mW\cdot cm^{-2}$. Exposure intensity of 20 $mW\cdot cm^{-2}$ led to an increment of rectal temperature approximately 0.3 ± 0.1℃ while further increase in the incident power density resulted in a noticeable elevation in deep body temperature after exposure time used here. It can also be seen, that the raising of ambient temperature from 20 to 30℃ in the most cases would greatly enhance rabbit heating because of a reduced rabbits ability to dissipate heat accrued from RFR exposure. In the absence of microwave exposure, rectal temperature exhibited by animals maintained at ambient temperature of 30℃ increased slightly (0.2± 0.1℃) over a 3-hour period.

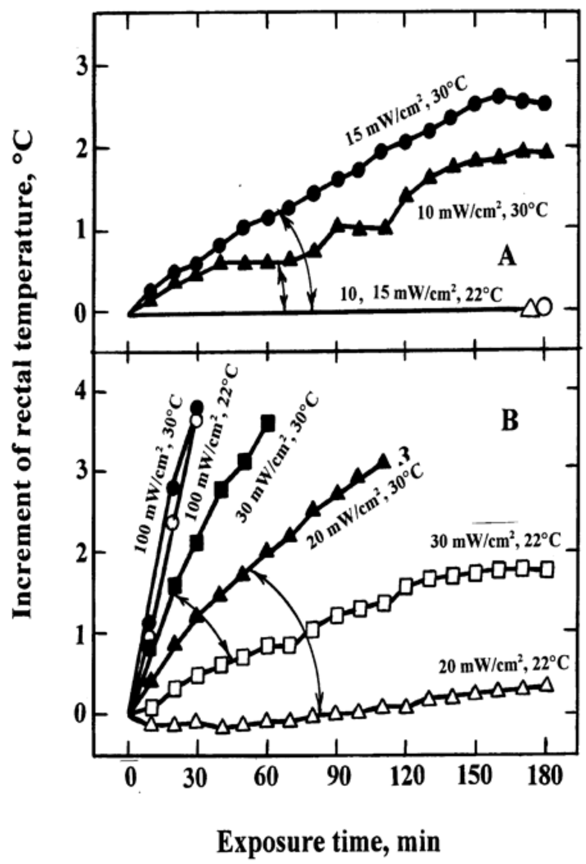

Fig. 1. The change in rectal temperature response exhibited by rabbits exposed to 7 GHz CW microwaves at various environmental temperatures and power flux density.

Basing on the data presented it can be concluded that the observed temperature increment after simultaneous action of high ambient temperature and RFR exposure was in most cases greater than that expected for additive effects of these factors. It means that the synergistic interaction between microwave energy and thermal load induced by high ambient temperature is observed. To estimate the effect of synergy quantitatively we used the synergistic enhancement ratio which can be determined by the ratio of temperature increments observed in experiments after simultaneous action of both factors ΔT(RFR, 30℃) to that expected for additive summation of thermal effects from microwaves alone ΔT(RFR, 22℃) and high ambient temperature ΔT(30℃) estimated for any identical duration of exposure:

$$k(\text{syn.}) = \Delta T(\text{RFR, 30℃}) / [\Delta T(\text{RFR, 22℃}) + \Delta T(\text{30℃})]. \quad (1)$$

It worth to note that the increment of rectal temperature exhibited by animals exposed to microwaves alone was estimated after irradiation at a comfort temperature (22℃). The synergistic enhancement ratio, determined by Eqn. 1, shows how many times temperature increment after simultaneous application of both modalities exceeds the sum of increments expected from individual action of each agent. In fact, the synergistic enhancement ratio is directly proportional to the angle between heating curves obtained at normal (22℃) and high (30℃) ambient temperatures.

To calculate the synergistic enhancement ratio we approximated experimentally obtained curves by straight lines. In other words, we did not take into consideration the reduction of heating effectiveness observed in some cases after a long irradiation and which might be related with operation of some additional mechanisms of temperature regulation. Moreover, the adaptation period of rabbit to the experimental conditions was taken into consideration. It can be seen (Fig. 1B) that colonic temperature was not increased immediately after the beginning of low intensity exposure but approximately after 1 hr. Therefore in our approximation we believe that the beginning of low intensity exposure was conditionally delayed for 30 min. That is why the values the synergistic enhancement ratio obtained here and published before [19] were somewhat different.

Fig. 2 shows the dependence of the synergistic enhancement ratio, calculated on the basis of Eqn. 1 and the results presented in Fig. 1, on the power flux density. It is clearly seen that the synergy takes place for some power densities while for others the interaction is small or only additive. It means that the synergistic interaction of microwave energy

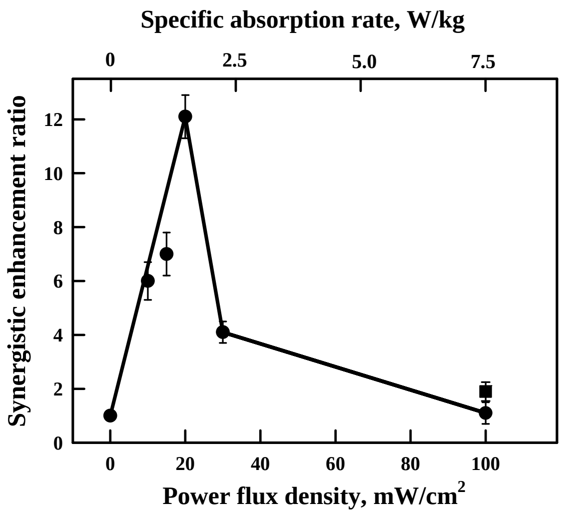

Fig. 2. Relationship between the synergistic enhancement ratio and power flux density after simultaneous action of microwave (7 GHz) exposure and high environment temperature (30℃) on rabbit heating.

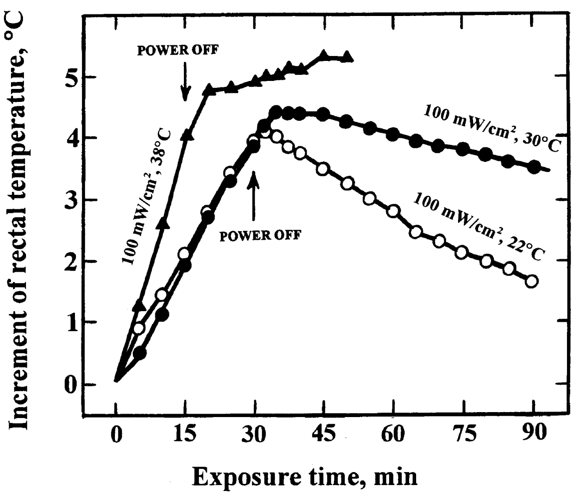

Fig. 3. The change in rectal temperature exhibited by rabbits exposed to RFR at 100 mW·cm^{-2} and various ambient temperatures: 22, 30 and 38℃. Arrows show the moment of microwave power off.

with high environmental temperature was observed for rabbits only within a definite ratio of incident power density of electromagnetic radiation. One can see that there is an optimal intensity at which the highest synergy is achieved.

In accordance with our previous investigations with unicellular organisms [4, 5], for a constant dose rate of ionizing radiation, the increase in the exposure temperature could result in an increase of synergy. Therefore it would be of interest to test this conclusion for rabbit heating. We measured the change in rectal temperature exhibited by rabbits exposed to RFR at 100 mW·cm^{-2} and various ambient temperatures. The results are shown in Fig. 3. As it can be seen, for this power flux density there is almost no difference in the efficiency of rabbit heating both at 22 and 30℃. Inversely, microwave exposure of rabbit at a higher ambient temperature (38℃) was more effective, the synergistic enhancement ratio, estimated by Eqn. 1, was equal to 1.9. This result is depicted in Fig. 2 by a square sign. It turned out that further investigation of the synergy for lower intensities of microwaves delivered at 38℃ was embarrassed because animals did not sustain this high environmental temperature for a long time. Nevertheless, the expected increase in a synergy with an increase of exposure temperature was fulfilled.

4. DISCUSSION

In this paper, basic features of synergistic effect between radio-frequency electromagnetic radiation and ambient temperature on rabbit heating have been revealed. The results show that for a constant ambient temperature the effectiveness of synergistic interaction is observed only inside a certain range of the power flux density. Moreover, within this range an optimal value can be indicated, at which the greatest synergistic effect can be achieved. Both increase and decrease in the power flux density from this optimal value resulted in a decrease of the synergy. It worth to note that the dependence of synergy on the intensity of the agents used in combination is well known fact for cellular systems of various origin [5, 21–23]. It is of interest that just such a dependence of synergy on the intensity of various physical agents was predicted by a mathematical model describing the synergistic effects of hyperthermia applied together with ionizing [24] or ultraviolet [25] radiations as well as with ultrasound [26] and some chemicals [27]. The results obtained here are in qualitative agreement with the model prognosis and would be useful to develop optimal regimens of thermoradiation action in cancer treatment as well as for further exploiting unified radiofrequency radiation safety standards.

It is known for a long time that different animals after combined action of RFR and high ambient temperature may be overheated more rapidly comparing with the RFR exposure at comfort conditions because the heat dissipation at a high ambient temperature is awkward [10,11,19,28,29]. Human beings and animals have similar physiological mechanisms of body heat homeostasis [30]. Therefore, one can expect the synergistic responses of man to the combined action of RFR and heat. The professional work at heavy heat exchange conditions is in a particular danger. Physical working load in the condition of microwave irradiation and high environmental temperature can also result to an additional rise in body temperature [17]. Thus, these data indicate that safety limits of microwave radiation should take into account the synergistic interaction of ambient temperature and RFR described here.

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