DETERMINATION OF HEAT EFFECT IN THE BIOSYNTHESIS PROCESS OF TETRACYCLINE

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One of the problems in the manufacture of antibiotics is removal of heat, liberated in the process of microorganism activity. This amount of heat determines the necessary surface of the cooling units in the fermenter and consumption of cooling water. The examined problem has attracted ever-increasing attention in recent years [1-5], since use of more concentrated nutrients and productive strains naturally leads to an increase in specific heat liberation in the biosynthesis process.

We carried out the determination of the amount of liberated heat in the biosynthesis process applied to a highly cultivated microorganism, a tetracycline producer, in a 3-m^3 fermenter (Fig. 1). The amount of liberated heat in the biosynthesis process (Q_{ferm}) is made up of heat liberated as a result of microorganism activity (Q_{bios}) and dissipation of energy during stirring (Q_{stirr}). The heat balance of the fermentation process can be expressed by the equation [1, 4, 5]: $Q_{ferm} = Q_{bios} + Q_{stirr} - Q_{ev} - Q_{surr}$ where $Q_{ferm} = Gc(t_2 - t_1)\tau$, G is consumption of cooling water (liters/h); c is specific heat capacity of water (kcal/kg · deg); t_1 and t_2 are temperatures of the cooling water at the entrance and exit of the fermenter housing (deg); τ is time (h). Q_{stirr} was determined from the consumption of energy for stirring, calculated from the voltage and measured current strength (without consideration of energy of idle motion). Temperatures at the entrance and exit of cooling water, and also at the entrance and exit of air from the fermenter, were measured with thermometers; the amount of water was measured with the measuring vessel and rotameter, and air consumption was measured with a rotameter.

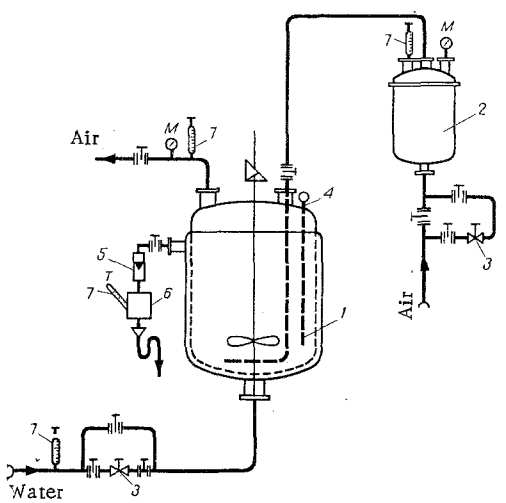

Fig. 1. Scheme of the unit for determination of heat effect: 1) fermenter; 2) air filter; 3) regulating valve; 4) resistance thermometer; 5) rotameter; 6) measuring vessel; 7) thermometer.

Heat consumption for evaporation of moisture $Q_{ev} = L(I_2 - I_1)$, where L is air consumption recalculated to the absolutely dry amount (kg/sec); I_1 and I_2 are the heat contents of air at the entrance and exit from the fermenter (kcal per 1 kg of absolutely dry air).

The amount of heat carried away by the leaving air was negligibly small: from 200 to 400 kcal/h; this exceeds literature data [4] by approximately two times. Heat losses to the surrounding medium, consequently given by a series of investigators [2, 3, 5], do not exceed 5%, which is what we assumed in the calculations.

The fermenter was charged with 1.8 m^3 of enriched nutrient medium, into the composition

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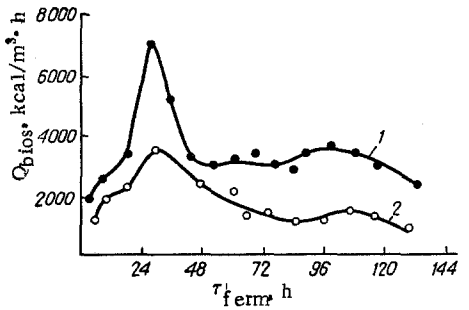

Fig. 2. Change in heat liberation in the biosynthesis process; 1) fermentation with a relative activity of 1; 2) fermentation with a relatively activity of 0.5.

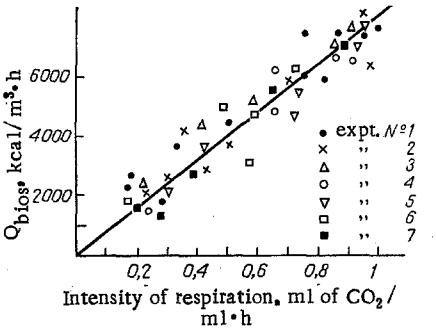

Fig. 4. Dependence between heat liberation and intensity of respiration in the tetracycline biosynthesis process in the period up to 50 h of development.

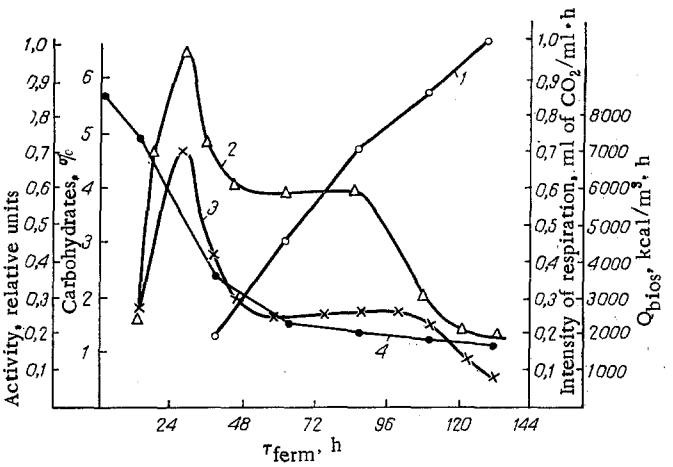

Fig. 3. Dynamics of change in a series of parameters in the tetracycline biosynthesis process: 1) activity; 2) intensity of respiration; 3) heat liberation; 4) carbohydrates.

of which entered about 6% carbohydrates and sperm whale oil, introduced regularly during the whole fermentation process. Air consumption in the biosynthesis process was varied from 0.5 to 0.8 m^3/min per 1 m^3 of medium. Intensity of respiration of microorganisms was determined by periodic measurements of the carbon dioxide gas concentration in air leaving the fermenter (using a VTI-2 gas analyzer).

Heat effect of stirring was clarified not only by dissipation of energy, but also directly. For this purpose the fermenter was charged with 1.8 m^3 of water and its initial and final temperature were measured after 2, 3, and 4 h of stirring in the absence of aeration and cooling. The amount of heat liberated by stirring, calculated by the heat balance equation, amounted to 1750 kcal/m^3 · h on the average. The value of Q_{stir} was varied from 1500 to 2000 kcal/m^3 · h in the fermentation process, which can be explained by aeration and an increase in viscosity of the culture liquid in the biosynthesis process.

The change in heat liberation with time for two operations having different final antibiotic concentration per unit volume is shown graphically in Fig. 2: the maximum (curve 1) and 50% lower (curve 2). We see that in both cases the maximum heat liberation is observed in the period between 20 and 50 h of fermentation, differing, however, in absolute value. After a lapse of 48-50 h of producer development heat liberation decreased sharply in both cases.

Maximum heat liberation due to microorganism activity (Q_{bios}), observed in the period between 20 and 50 h of fermentation, can vary from 3000 to 8000 kcal/m^3 · h, but because of its relative brevity it is reflected very insignificantly on the average indices. Thus, statistical treatment of experimental data obtained upon analysis of heat liberation in the tetracycline biosynthesis process showed that Q_{bios} amounts to 2000± 160 kcal/m^3 · h on the average for all operations, while Q_{ferm} (with consideration of the heat effect of stirring) amounts to 3830 ± 173 kcal/m^3 · h.

Curves of changes in a series of parameters during the fermentation process are presented in Fig. 3. As is seen, the maximum heat liberation coincides with the period of maximum intensity of respiration and the fastest rate of carbohydrate requirement. The character of this dependence in the range up to 50 h of fermentation is linear, as is seen from Fig. 4. However, subsequently the rate of hydrocarbon requirement decreases significantly, while the intensity of respiration is retained at quite a high level approximately up

to 80-85 h of development. Evidently, during this time period the growth process continues, although not as intensely as in the first period of development. Determination of the weight of mycelles in the described experiments (which could have confirmed the given hypothesis) was interfered with by the heterogeneity of the fermentation medium used; however, it was established upon using an analogous homogeneous medium in flasks on a shaker that the growth of producer continues up to 70-80h of development.

Thus, as experiments show, a brief increase in heat liberation occurs in the period of intensive development of the tetracycline producer (up to 50 h); a virtually linear dependence is observed between its intensity and respiration of the microorganism. These data agree with results obtained in the study of interrelations between oxygen requirement, respiration, and heat liberation in the process of cultivation of yeasts and bacteria [4]. However, in our case this dependence is disturbed in the second period of fermentation, upon advance of the phase of active antiobiotic formation.

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