Fire and explosion hazard of some drugs capable of intense exothermic decomposition

Do Thanh Hung

Annotation

In many industries, especially in the chemical industry, solid organic substances are widely used. In the pharmaceutical field, in order to change the pharmacokinetic properties of drugs, various functional groups are added to the molecule of a substance during synthesis, including those that can lead to an increase in the fire and explosion hazard of the final product. In the production of drugs, there is often a risk of danger, in particular, during the drying and grinding stage, fine organic dust can form in the air of the working area. Drugs at this stage often form explosive dust-air mixtures, which, when colliding with factors such as strong heat sources, ular and friction sparks, static electricity discharges, etc., can cause an explosion.

In this study, within the framework of the Strategy for the Development of the Medical and Pharmaceutical Industry until 2025 (Decree of the Government of the Russian Federation dated December 28, 2012 No. 2580-r), substances obtained from the Federal State Unitary Enterprise "SSC NIOPiK" were studied: (2R)-2-amino-3 - hydroxypropanoic acid (“D-serine”), (R)-4-amino-3-isoxazolidinone (“D-cycloserine”), 4-[[4-[(3-Oxo-1,2-oxazolidin-4 - yl)iminomethyl]phenyl]methyliden amino]-1,2-oxazolidin-3-one (Terizidone), (RS)-2-(2-oxo-4-phenylpyrrolidin-1-yl) acetamide (Phenylpiracetam) and p-chloro-nitrostyrene (“PPB1”). All substances are drugs, PPB1 is an intermediate in the synthesis of the drug baclofen. D-serine can act as an independent drug, but is more often used in the process of D-cycloserine synthesis. The structure of three compounds contains nitro groups and an isoxazolidine group. This study is devoted to a comprehensive study of the isoxazolidine group, which affects the mechanism of thermal decomposition of a substance.

Scientific novelty

In the work, for the first time, thermal analysis was carried out for five substances, their behavior was studied when heated both in an oxidizing atmosphere (air) and in an inert one (helium or nitrogen).

For all substances, for the first time, the values of the temperature of the beginning of exothermic decomposition (t_{neer}) were established.

For four substances, the kinetic parameters of the initial stage of thermal decomposition were determined for the first time and an assumption was made about its mechanism.

For four substances, the exothermic effects of the initial stage of thermolysis were calculated for the first time.

It has been established for the first time that the [–C–O–N–] group in a five-membered heterocycle is an explosiphoric group.

For all substances, for the first time, indicators of fire and explosion hazard in the state of airgel and aerosol were determined. It is shown that the regularities of the classical theory of thermal explosion are applicable for calculating the flash points of two substances.

Using the method of critical pressures, it is shown that three substances are sensitive to mechanical stress.

For five substances, the enthalpies of formation and heat of combustion were obtained for the first time by calculation methods.

Theoretical and practical value

In the theoretical aspect, the work explores previously unexplored or insufficiently studied properties of compounds - thermal stability, sensitivity to mechanical stress, kinetic parameters of decomposition of these substances, for the first time a number of important indicators of fire and explosion hazard are determined in the work.

The results of studies on thermal decomposition and fire and explosion hazard obtained during the work were transferred to the Federal State Unitary Enterprise "SSC NIOPiK" to create technological regulations for the production of the studied

compounds in terms of safe operating modes of equipment and safe operation of production, to establish and clarify the categories of industrial buildings in terms of fire and explosion hazard, categories of explosion hazard technological blocks, which is confirmed by the act of implementation.

Key points for the thesis presentation:

Results of experimental studies in the field of fire and explosion hazard of D-serine, D-cycloserine, terizidone, p-chloro-nitrostyrene and phenylpiracetam.

Calculation results of fire and explosion hazard indices of D-serine, D-cycloserine, terizidone, p-chloronitrostyrene and phenylpiracetam.

Results of thermal analysis of D-serine, D-cycloserine, terizidone, p-chloro-nitrostyrene and phenylpiracetam by differential thermal analysis and differential scanning calorimetry.

Results of calculation of kinetic parameters based on experimental data and mechanism of thermolysis of D-cycloserine and terizidone.

Temperature values for the onset of exothermic effects of D-cycloserine, terizidone, as well as for p-chloronitrostyrene and phenylpiracetam.

Results of calculation of thermodynamic parameters of combustion using a specialized software package for D-cycloserine, terizidone.

Results of calculation of autoignition (flash) temperatures for D-cycloserine, terizidone.

The results of the calculation of the enthalpy of combustion according to the Hess law and confirmation of the correctness of the calculation according to the Konovalov-Khandrik method for D-serine, D-cycloserine, terizidone, p-chloro-nitrostyrene and phenylpiracetam.

The results of the calculation of the enthalpy of formation in the gaseous phase by additive methods and using the MOPAC package for D-cycloserine, terizidone, as well as for D-serine, p-chloro-nitrostyrene and phenylpiracetam.

Results of studies of the mechanical sensitivity of D-serine, D-cycloserine, terizidone, p-chloro-nitrostyrene and phenylpiracetam.