Milovidov Pavel Dmitrievich

«Fire and explosion hazard of new drugs with composite chemical structure»

Abstract

In the manufacture of dosage forms, a significant part of powdered substances has combustible properties and/or is capable of explosion. The potential danger is realized at various technological stages associated with the formation of aerogels and air suspensions: during the preparation of raw materials, mechanical processing, storage and transportation, and especially during thermal processes, for example, with various types of drying. Such processes are particularly dangerous and require special advance measures to prevent fires and explosions. The dissertation research is devoted to a comprehensive study of the thermal stability and fire- and explosion-hazardous properties of eight new drugs with composite chemical structures. The relevance of the work is due to the widespread introduction into pharmaceutical production of composite chemical compounds with potential fire and explosion hazards in technological processes associated with the formation of aerogels and air suspensions, while the lack of data on the individual properties of these substances requires special research to ensure industrial safety.

The purpose of the work is a comprehensive study of the thermal stability, fire- and explosion-hazardous properties of new drugs with composite chemical structures for the subsequent introduction of scientifically sound data into technological regulations in production.

Work objectives:

1. To conduct a thermoanalytical study of substances using synchronous thermogravimetry (TG) and differential thermal analysis (DTA), as well as using differential scanning calorimetry (DSC) at various heating rates.

2. To study the kinetics of thermal decomposition of compounds, determine the activation energy and propose mechanisms of destruction using modern experimental and computational methods.

3. Determine the main fire and explosion hazard indicators experimentally and by calculation methods.

4. To establish the influence of functional groups and molecular structure on the fire-hazardous properties of air suspensions

5. Calculate the thermochemical characteristics (enthalpy of formation, heat of combustion) of the studied compounds using computational methods.

As a result of the research, the key characteristics of the compounds under study have been established. For preparations containing hydrochloride groups (maritupirdine, ravidasvir, umifenovir), the initial stage of thermal decomposition occurs in the temperature range of 110-250 ° C with HCl cleavage, which is confirmed by a mass loss of 5-12%, corresponding to the theoretical content of hydrogen chloride in the molecules. The activation energy of these processes is 56-76 kJ/mol, which indicates their thermal instability.

For phthalocyanine compounds (teraphthal, photosense), the temperature of the onset of intensive decomposition is 370-410 °C, and the activation energy reaches 142-205 kJ/mol, which confirms their high thermal stability.

When studying the fire and explosive properties, it was found that the maritupirdine air suspension poses the greatest danger with lower concentration limit of flame propagation of 48 g/m3 and belongs to the 2nd hazard class. The dusts of ravidasvir and thiosense have lower concentration limit of flame propagation of 102 and 115 g/m3, respectively, and are classified as hazard class 4. Based on experimental and calculated data teraphthal and photosense are classified as difficult-to-burn substances, while the remaining six compounds are classified as combustible materials.

The thermochemical characteristics of the compounds, including the enthalpy of formation and heat of combustion, which range from -16.9 to -34.6 MJ/kg, have been calculated. An improved technique for modeling the molecular structure of hydrochloride-containing compounds has been developed, which has significantly improved the accuracy of calculations.

The following provisions are put forward for protection:

1. Thermoanalytical characteristics of substances obtained using modern research methods TG-DTA; DSC;

2. Experimentally established kinetic patterns of thermal decomposition of seven organic compounds, including activation energies, pre-exponential factors;

3. Experimentally established temperatures of the onset of intense decomposition, ignition and auto-ignition temperatures, the lower concentration limit of flame propagation, determination of the flammability group;

4. Patterns of the complex influence of various functional groups, halogens, and inert elements N and O in the structure of matter on the lower concentration limit of flame propagation of dusts;

5. Thermochemical characteristics for eight compounds, such as enthalpies of formation in the gas and solid phases, calorific values of combustion, calculated by several different methods using both quantum semi-empirical methods and reference additive techniques.;

6. Assumption of the mechanism of the initial stage of thermal decomposition for five compounds, identification of patterns.

The obtained results have been implemented into production practice at NIOPIK JSC and API-technology LLC and are used in the development of fire safety measures and ensuring fire and explosion safety of the production of the studied compounds.