IMPROVEMENT METHODS RECEIPTS HYDROCHLORIC ACID SEMICARBAZIDE FROM HYDRAZINE HYDRATE AND UREA IN INDUSTRIAL TERMS AND CONDITIONS

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Semicarbazide (SC) is the starting material for the synthesis of such medications as furacillin (also known as nitrofurazone or nitrofural), nitrofurantoin (furadonin), furazolidone, phenytoin (diphenin, dilantin – a derivative of hydantoin), a number of sulfanilamide derivatives and antidiabetic drugs. SC and its derivatives serve as universal reagents for the synthesis of various acyclic and heterocyclic nitrogen-containing compounds, such as semicarbazones, azapeptides, hydantoins, pyrazoles, triazines, triazoles, oxadiazoles, pyrimidines and azamacrocycles. This is why high-purity SC is required in pharmacy. In addition, in the pharmaceutical chemistry SC is used as a qualitative reagent for the analysis of aldehydes and ketones. It reacts with them to form semicarbazones - crystalline connections with clear temperature melting that are convenient for identifying carbonyl connections.

One of the methods for producing SC, both in the laboratory and in industry, is the reaction of urea with hydrazine hydrate (HH) at a temperature of 90-120 °C. We have shown [1] that with a stoichiometric ratio of components and vigorous stirring at the boiling point of the mixture (103-105 °C), the yield of SC does not exceed 60% of the theoretical value. This is explained by the fact that some of the HH is removed from the reaction zone along with ammonia. In addition, in the final stages of the process, the system's density increases significantly because the SC crystals are highly dispersed. Nevertheless, the synthesis efficiency can be increased to a product

yield of 90-92% by increasing the excess urea to 3-3.5 times the stoichiometric amount. This is technologically justified, since urea costs 15-20 times less than HH.

The synthesis of SC was carried out in a two-liter flask on an oil bath. The SC was filtered under vacuum, washed with cold water, and dried at 80 °C. The major drawbacks of this method are the high system resistance during stirring and the difficulty of extracting the product from the flask without diluting it with water. Since the solubility of SC in ice water is 4.5 g/100 ml, an additional 10-15% of the product is lost after purification. This method is suitable for a one-time process. If large quantities of SC are required, an alternative is to ensure a continuous process. When the synthesis is 20-25% complete and a precipitate forms in the flask that impedes stirrer rotation, half of the contents should be poured off, cooled and filtered. Then rinse with hot water. Mix the water after washing with the filtrate, add glycerol and urea in a 1.5-fold excess of the stoichiometric ratio, and then return to the flask. Rinse the SC a second time with cold water and dry. Although this method requires additional time and energy to evaporate excess water, the continuous nature of the process allows for the resolution of several process issues during the synthesis and increases product yield. The synthesis was carried out in a 5-L flask heated in an oil bath at 120° °C. After processing 20 kg of SC and 42 kg of urea, the SC yield was 85% of the theoretical value. If this method is used for synthesis in a reactor, efficiency can be increased by absorbing ammonia and hydrazine with nitric acid, with subsequent utilization of the resulting products.

Both methods require additional purification of the urea from biuret , which forms when urea is heated and precipitates. Its amount does not exceed 0.5-1 % and is usually not a hindrance to further processing of the urea. However, purification by reprecipitating of the urea from hot water is insufficient to obtain a pure product. It is necessary to dissolve the urea in hydrochloric acid, reprecipitate the hydrochloric acid urea, then remove the hydrogen chloride with alkali and reprecipitate it again from hot water. Since SC oxidizes during storage, its stable form in the form of semicarbazide hydrochloride (SCH) is usually used as a starting component for synthesis. Therefore, to obtain high-purity SC, it must be converted to SCH, purified by crystallization, and isolated by the action of alkali.

Thus, the following conclusions can be drawn:

1. For a small amount of SC, its synthesis should be carried out with a significant stoichiometric excess of urea, for production - in a ratio of 1:1.5 and to a conversion degree of 20-25 % in a continuous process.

2. In both cases, partial contamination of the SC with biuret is observed, which is removed by converting the product into hydrochloric acid followed by reprecipitation.

References:

1. Arnaut K.A., Lozhychevska T.V., Savin S.M., Kiose O.O., Pluzhnyk-Gladyr S.M. Improvement of the synthesis method of semicarbazide hydrochloride in laboratory conditions // Міжнародна Internet-конференція «Modern chemistry of medicines» - м.Харків, 7 листопада 2025 – С. 13.