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## ON THE POSSIBILITY OF COMBINING DIMETHYLAMINOETHANOL WITH SODIUM SUCCINATE IN A SINGLE DOSAGE FORM

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**Introduction.** In recent times, cognitive impairments have spread significantly due to many factors, in particular, due to the beginning of full-scale armed aggression by the Russian Federation. The creation of new effective and safe combined medicines with dimethylaminoethanol and sodium succinate is a crucial task of modern medicine and pharmacy. For co-use of dimethylaminoethanol and sodium succinate, it is necessary to study their physicochemical properties.

**Purpose of the work** is to study the possibility of combining dimethylaminoethanol with sodium succinate in one dosage form.

**Materials and methods.** The object of study is dimethylaminoethanol and sodium succinate. The crystallographic properties of the substances were studied according to the SPhU using optical crystallography and photomicrography using a Ulab XY-B2T LED microscope (China). Thermogravimetric analysis was carried out on derivatograph: "ShimadzuDTG-60" derivatograph (Japan) with a platinum-platinum rhodium thermocouple while heating the samples in aluminum crucibles (temperature regime from 17 to 200°C).

**Results.** The study of the crystallographic properties of dimethylaminoethanol and sodium succinate made it possible to predict the possibility of their combination in one dosage form. Thanks to the further study of the physical and chemical properties of dimethylaminoethanol and sodium succinate using thermogravimetric analysis, it was found that they are thermally stable compounds. According to the results of the obtained derivatograph data, production of the dosage form should take place at a temperature not higher than 105°C.

**Conclusions.** According to the crystallography and derivatograph study of dimethylaminoethanol and sodium succinate substance and the mixture of dimethylaminoethanol-sodium succinate, it should be noted that the mixture of dimethylaminoethanol and sodium succinate is a mixture of active substances that do not interact with each other and can be in the same dosage form in the form of tablets obtained by the direct compression, or sachets.

**Keywords:** dimethylaminoethanol, sodium succinate, crystallography, derivatograph, dosage form.

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### ЩОДО МОЖЛИВОСТІ ПОЄДНАННЯ В ОДНІЙ ЛІКАРСЬКІЙ ФОРМІ ДИМЕТИЛАМІНОЕТАНОЛУ З НАТРІЄМ СУКЦИНАТОМ

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У сучасних умовах значного поширення порушень когнітивних функцій, зокрема через початок повномасштабної збройної агресії РФ, актуальним є створення ефективного та безпечного комбінованого лікарського засобу. Мета дослідження полягала у визначенні можливості поєднання диметиламіноетанолу та натрію сукцинату в одній лікарській формі. Об'єктами дослідження стали ці дві субстанції, а методами – оптична кристалографія і мікрофотографування та термогравіметричний аналіз. Встановлено, що диметиламіноетанол і натрій сукцинат є термічно стабільними у відповідних температурних діапазонах. Дослідження показали, що ці речовини не утворюють стійкого комплексу та можуть бути сумісними в одній лікарській формі у вигляді таблеток, одержаних методом прямого пресування, або саше.

**Ключові слова:** диметиламіноетанол, натрій сукцинат, кристалографія, дериватографія, лікарська форма.

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## Introduction

The problems of disorders of cognitive functions have always been given great importance, but interest in the problem of cognitive disorders has recently increased significantly. The relevance of this issue is due to the discovery of pathogenetic mechanisms of impaired cognitive functions and the increase in the percentage of older people among the population [1; 2]. However, in Ukraine, this problem has a more significant impact due to the full-scale armed aggression of the Russian Federation. According to the results of the study, it was found that 63.7% of Ukrainians have medium and high levels of stress, and 65.9% of Ukrainians consider the war to be a traumatic experience that leads to impairment of cognitive abilities [3]. Mobilization of all possible means to ensure high combat capability of servicemen is also an urgent problem today. This requires a high level of provision of the personnel of the Armed Forces of Ukraine with the widest possible range of medical and preventive means [4].

Despite constant efforts to optimize the treatment of cognitive impairments, this problem is urgent, due to the fact that the pharmaceutical market mainly presents stress-protective and anxiolytic drugs, which have a number of side effects and relative toxicity. Therefore, the development of new highly effective and safe medicines is an important issue. It is expedient to create a new combined medicine, which, in addition to the main active substance, contains an antioxidant, which leads to potentiation of the pharmacological effect, dose reduction, and reduction of side effects of the main active substance, and in some cases to their avoidance [5].

The broad-spectrum antioxidant thiotriazoline, which has high activity and practically does not cause side effects, is important in this regard. Thiotriazoline has antioxidant, anti-ischemic, membrane-stabilizing, anti-arrhythmic, anti-inflammatory, antiviral and stimulating cell regeneration activity [6]. However, the antioxidant dimethylaminoethanol in combination with sodium succinate is also interesting for study.

Dimethylaminoethanol is a precursor to choline, which is needed for the synthesis of acetylcholine, a neurotransmitter involved in the transmission of signals from nerve cells [7]. Dimethylaminoethanol is also interesting because it has antioxidant properties, which in turn helps to protect the brain from oxidative stress. The role of sodium succinate in the energy metabolism of cells has been studied, but its effect on cognitive functions is not as widely studied, however, this substance is associated with processes that contribute to increased energy production in cells. This can potentially be beneficial for cognitive abilities [8; 9].

For co-use of dimethylaminoethanol and sodium succinate, it is necessary to study their physicochemical properties, thanks to which it will be possible to solve the question of the conditions under which they do not form a stable complex to create a dosage form. The following study methods were chosen: crystallography to study the properties of powders and thermogravimetric analysis to determine the thermal properties of substances [10–12].

**Purpose of work** – study on the possibility of combining dimethylaminoethanol with sodium succinate in one dosage form.

## Materials and methods

The substances of dimethylaminoethanol (producer – USA), sodium succinate (Anhui Xingzhou Medicine Food Co., Ltd, China), dimethylaminoethanol-sodium succinate mixture prepared at the Department of Pharmaceutical, Organic and Bioorganic Chemistry of Zaporizhzhia State Medical and Pharmaceutical University were used as objects of the study. The crystallographic properties of the substances were investigated using optical crystallography and photomicrography using a Ulab XY-B2T LED microscope (China). Thermographic analysis was carried out using the Shimadzu DTG-60 (Japan) derivatograph with a platinum-platinum rhodium thermocouple when samples were heated in aluminum crucibles (from 17 °C to 200 °C).  $\alpha$ -Al<sub>2</sub>O<sub>3</sub> was used as a reference substance. The heating rate was 10 °C per minute. The weight of the studied samples was from 14.21 mg to 35.72 mg. The derivatograph graphically recorded the received data in the form of T, DTA, TGA curves. The T curve on the derivatogram reflects the change in temperature, and the TGA curve shows the change in the mass of the sample during the study period. The DTA curve demonstrates the differentiation of thermal effects, contains information about endothermic and exothermic maxima, and can be used for qualitative assessment of the derivatogram [13].

## Results

The crystallographic studies of dimethylaminoethanol and sodium succinate substance and a mixture of dimethylaminoethanol-sodium succinate in a 1:1 ratio were carried out to determine the shape and size of powder particles. The study on the shape and size of particles was carried out using the Inter Video WinDVR computer program. The study results are shown in figures 1, 2, 3.

According to crystallographic data, it was established that dimethylaminoethanol is a white polydisperse crystalline powder with an average particle size of 50  $\mu$ m. The shape of the crystals is isodiametric, in the form of lamellar polyhedra and their fragments.

The study of the crystallographic properties of the sodium succinate substance powder showed that it is a white polydisperse crystalline powder. Crystals of anisodiametric form in the form of small and large elongated prisms and their fragments with an average size of 65  $\mu$ m.

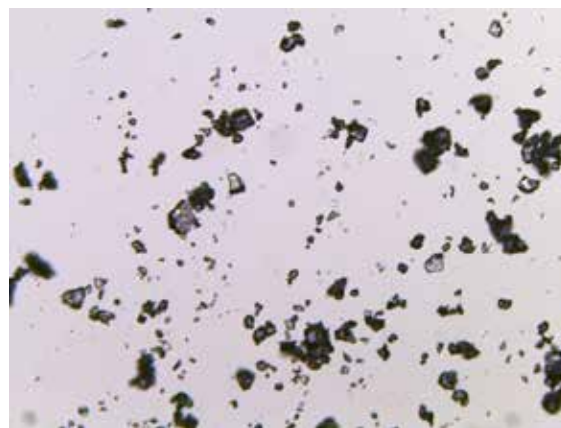


Fig. 1. Photomicrography of dimethylaminoethanol substance powder (magnification  $\times 400$ )

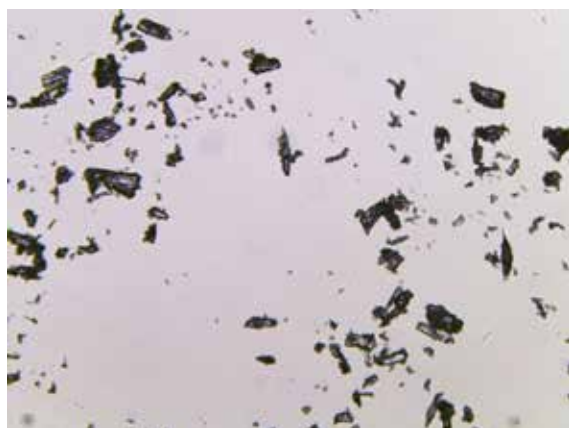


Fig. 2. Photomicrograph of sodium succinate substance powder (magnification ×400)

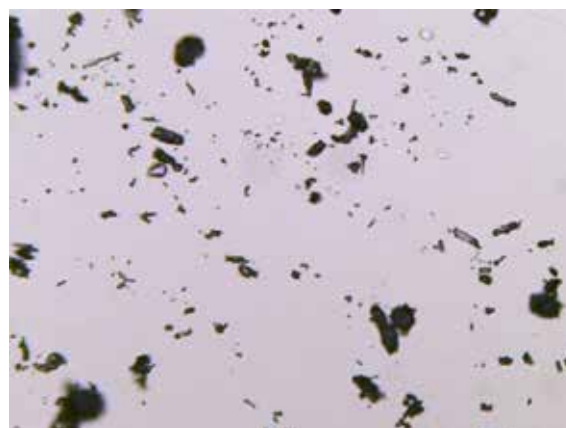


Fig. 3. Photomicrograph of sodium succinate and dimethylaminoethanol mixture substance powder (magnification ×400)

The study of the crystallographic properties of dimethylaminoethanol and sodium succinate substances mixture made it possible to predict the possibility of obtaining tablets by the method of direct compression or sachets.

Thermogravimetric studies of dimethylaminoethanol, sodium succinate and their mixture (1:1) were also carried out. The results are shown in figures 4, 5, 6.

According to the given data (Fig. 4), the active substance dimethylaminoethanol is a thermally stable compound in the temperature range from 17°C to 113 °C. At the 4th minute of the experiment at a temperature of 56.24 °C, the weight of the test sample decreased by 1.62% (2.23 mg), after which an increase in the endothermic effect and a gradual decrease in the weight of the sample were observed. At the 9th minute of the experiment: the mass loss at a temperature of 113.2 °C was 5.98% (0.85 mg). At the 18th

minute of the experiment: at a temperature of 202.16 °C, the mass of the sample decreased by 6.62% (0.94 mg), and at the end of the experiment, at a temperature of 250.25 °C, the mass of the sample changed by 7.6% (1.08 mg).

Thermogravimetric study of sodium succinate (Fig. 5) showed that this sample is a relatively thermally stable compound in the temperature range from 20 °C to 142 °C. The mass of the studied sample was unchanged until the twelfth minute of the experiment at a temperature of 142.18 °C. At 18 minutes, a gradual decrease in mass began and the loss was 8.12% (2.9 mg). Later the dynamics of sample mass reduction increased rapidly and at the 23rd minute of the experiment, the mass loss was 90.76% (32.42 mg).

The derivatogram of the mixture of dimethylaminoethanol and sodium succinate (Fig. 6) demonstrates the similar nature of the thermal effects of individual

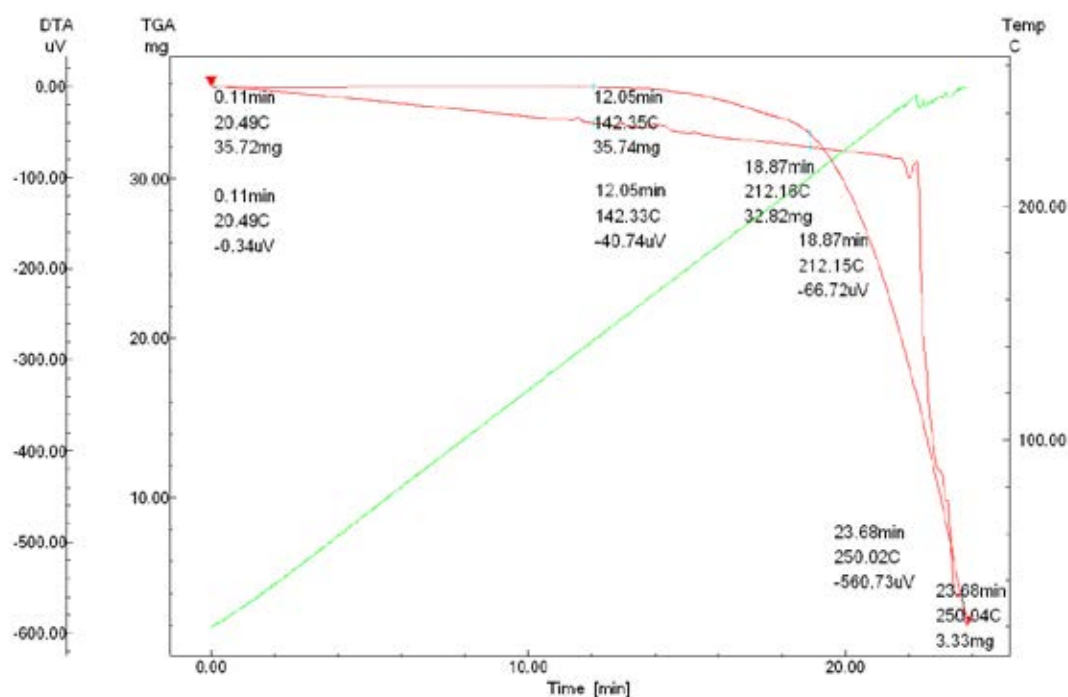


Fig. 4. Derivatogram of dimethylaminoethanol

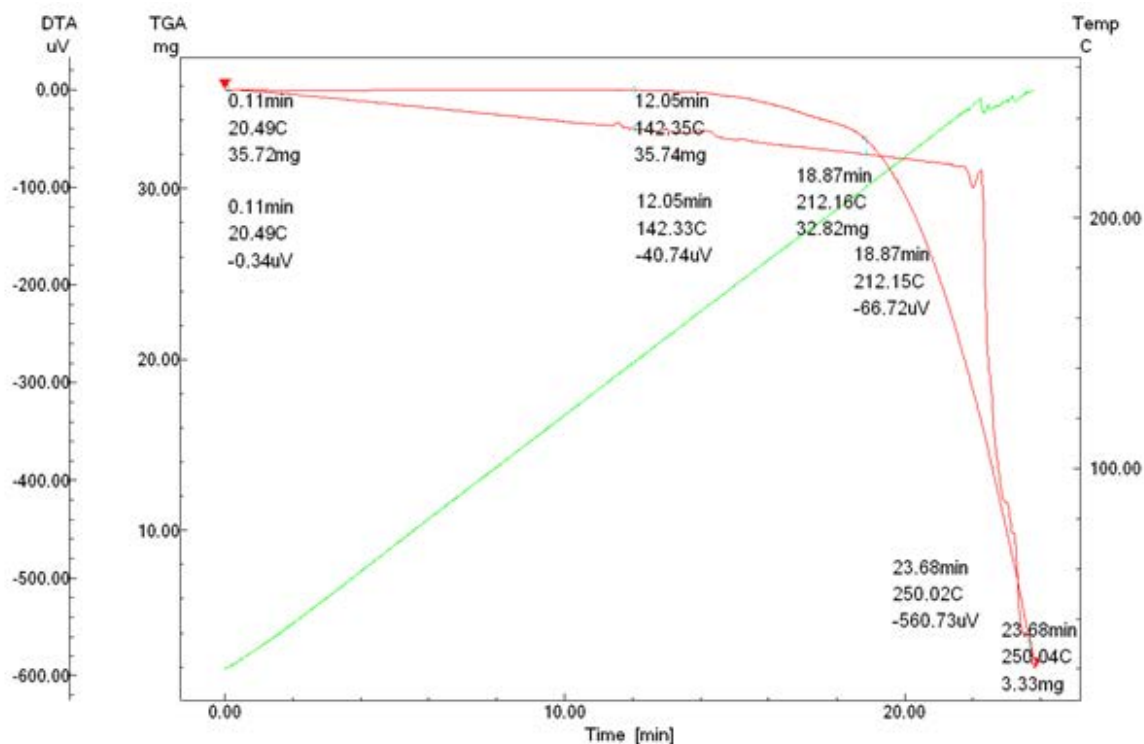


Fig. 5. Derivatogram of sodium succinate

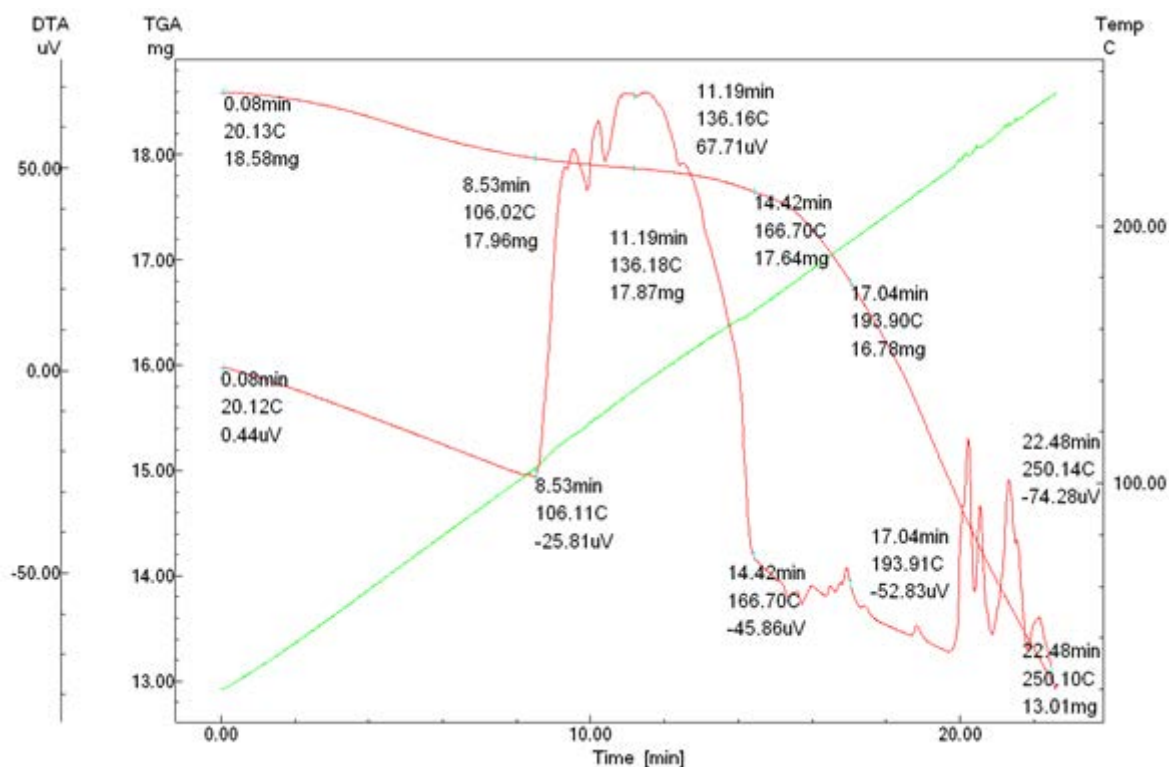


Fig. 6. Derivatogram of sodium succinate and dimethylaminoethanol mixture

ingredients of the mixture, which indicates the absence of interaction between the components. At the 8th minute of the experiment at a temperature of 8.53 °C, the mass change was 3.34% (0.62 mg). At the 11th minute of the experiment at a temperature of 136.18 °C, the mass change was 3.88% (0.72 mg). At the 14th minute of the

experiment at a temperature of 166.7 °C, the mass loss was 4.9% (0.91 mg), and already at the end of the experiment at a temperature of 250.10 °C, the change in the mass of the sample was 29.98% (5.57 mg). Thus, according to the thermogravimetric study results, it was found that when heating a mixture of dimethylaminoethanol with sodium



succinate to 105 °C, the substances remain in the form of powders, and with further heating, the mass of the sample decreases. The obtained data indicate that it is possible to combine dimethylaminoethanol and sodium succinate in one dosage form in the form of sachets or tablets, and in the technological process, operations can be carried out at a temperature of up to 105 °C.

### Discussion

The modern range of stress-protective, anxiolytic and nootropic drugs does not always meet all the requirements of doctors. This is mainly due to a number of side effects and relative toxicity [14; 15]. In modern medical practice, combined medicines are used, which include the main active substance and antioxidants, which leads to potentiation of the pharmacological effect, dose reduction, and reduction of side effects, and in some cases to their prevention. This necessitates the creation of new highly effective and low-toxic combined medicines that contain an active substance and an antioxidant. Succinate is associated with processes that contribute to increased energy production in cells. This property can be useful for cognitive functions [16].

The results of crystallographic studies of substances confirm that a mixture of dimethylaminoethanol and sodium succinate in a ratio of 1:1 can be combined in one solid dosage form.

According to the data of thermogravimetric studies, it was possible to determine the temperature (up to 105°C), up to which it is expedient to perform technological operations related to the manufacture of a dosage form containing a mixture of dimethylaminoethanol-sodium succinate (1:1).

### Conclusions

1. Study of physico-chemical indicators of dimethylaminoethanol and sodium succinate substances by crystallography allowed us to predict the possibility of obtaining tablets by direct compression or sachets.

2. It was found that the mixture of dimethylaminoethanol and sodium succinate (1:1) is a mixture of active substances that do not interact with each other, which makes it possible to combine them in one dosage form.

3. After analyzing the derivatograph data of dimethylaminoethanol and sodium succinate substance, mixture of dimethylaminoethanol-sodium succinate (1:1), it was established that in the technological process of manufacturing dosage forms it is advisable to carry out technological operations at a temperature of up to 105 °C.

**Prospects for further studies** – creation of a new combined dosage form that will exhibit nootropic properties and is planned for use in sleep disorders after stress, treatment of chronic fatigue syndrome, and combined therapy to increase the effectiveness of antidepressants.

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