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The study of technological properties of the granulated materials based on dry oat extract and quercetin obtained by wet granulation in a fluidized bed.

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Abstract: Investigation of technological properties of active pharmaceutical ingredients and intermediate products is essential part of manufacturing of any medicines. The focus of study was on technological properties of granulated materials obtained from dry oat extract and quercetin in order to develop new solid dosage. Microscopy of dry oat extract, different composition of granulated materials was performed. In order to obtain detailed information of technological properties of granulated materials bulk density, flowability, residual moisture and fractional composition was studied. Collected data allow us to predict that wet granulation in a fluidized bed is suitable method for dry oat extract and quercetin for obtaining granulated materials with good technological properties. Thus, study shown that granulated materials based on dry oat extract and quercetin are ready for tableting process.
Keywords: dry oat extract, quercetin, granulated materials, wet granulation in a fluidized bed, tableting process.

Introduction:

The problem of chronic stress and fatigue as a factor in the development of depression is a leader in somatic pathology of modern society[1]. On a par with those in the global pharmaceutical market is increasing the demand for drugs with adaptogen and tonic activity based on natural raw materials[2-3].So, expanding the range of drugs based on natural ingredients, creating a highly efficient solid dosage form of plant origin remains an urgent task for modern Pharmaceutical Industry.

Creation of original drugs - it is a separate, very serious link of pharmaceutical science and practice. Development of any dosage form requires a consistent and detailed study of all active pharmaceutical ingredients within its structure. Moreover research of intermediates products is also required additional study in order to give a proof of using some auxiliary substances during process operations. So, in order to develop a solid dosage form with adaptogen and tonic activity, we carried out a wide range of studies of dry oat extract and quercetin, which gave us the opportunity to plan the future course of research. The next step was the development of composition and technology of granulated materials as an intermediate product of tablets production, and its further investigation. It is known that the size and shape of the particles of the granulate influences such factors as content uniformity, the average weight of the tablet, the tablet mass delamination during tableting, resistance to crushing tablets and disintegration. Therefore, to obtain high quality tableting mass, we used the method of production of granules in a fluidized bed. This is due to the fact that this method allows combining the operations of mixing, granulation, drying, and powdering in a single apparatus, thus being the most uniform and least time consuming. The main advantage of the chosen method is to obtain granulated

materials with optimal technological properties[5-6]. The purpose of this study was to investigate the technological properties of granulated materials in order to create a tablet based on the dry extract of oats and quercetin. Study was conducted on pharmaceutical plant in Ukraine PJSC SIC "Borshchahivskiy CPP" which has fully implemented the international standards in quality (GMP, ISO 9001).

Objects and Methods:

The objects of study were quercetin (in recalculation on 100% dry matter), dry extract of oats, granulated materials. Methods: microscopic, organoleptic, technological study. The study used the following equipment: fluidized bed granulator (Unilab-5-DJ, Huttlin company), microscope (Axioscope 40, Carl Zeiss company). The initial stage of our work was determination of the size and shape of the powder particles of dry oat extract using the method of light-optical microscopy. The result obtained from microscopy is available (Fig. 1). The data obtained indicate that the powder of dry oat extract has transparent yellowish-brown color particles, which represent polydisperse crystalline system of anisodiametric type.

As we can see, there are majority of different geometric shapes and sizes of powder particles which were detected by microscopy; so, we can consider that powder particles of dry oat extract is polydisperse. This, in turn, may indicate a poor flowability of the powder.

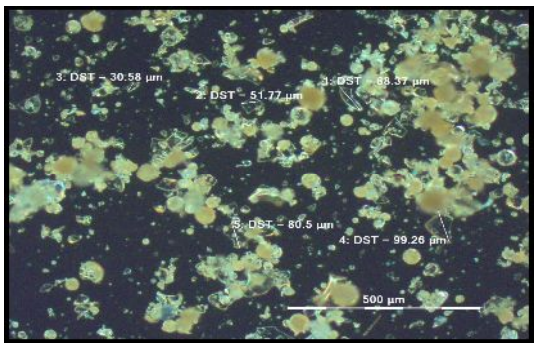

Figure 1: Results of microscopy of powdered dry oat extract

Result and Discussion:

To solve the problems we have designed and studied a series of three granulated materials (tableting mass), which have the same composition of active pharmaceutical ingredient, and the same list of auxiliary substances with varying their contents quantitatively.

Table 1: Composition of tableting mass

Ingredients of tableting mass	quantitative content					
	quantity, %			quantity per tablet, mg		
	1	2	3	1	2	3
quercetin (in recalculation on 100% dry matter)	3,64	3,64	4,00	40,00	40,00	40,00
Dry oat extract	9,09	9,09	10,00	100,00	100,00	100,00
citrus pectin	36,36	36,36	30,00	400,00	400,00	400,00
glucose monohydrate	33,05	33,05	36,35	363,50	263,50	363,50
sugar	14,55	14,55	16,00	160,00	160,00	160,00
Flavours powder (orange)	0,14	0,14	0,15	1,50	1,50	1,50
talcum powder	2,73	2,73	3,00	30,00	30,00	30,00
magnesium stearate	0,44	0,44	0,50	5,00	5,00	5,00
Total	100,0	100,0	100,0	1100,0	1000,0	1000,0

Bulk density, flowability, residual moisture and fractional composition of granulated materials were studied. In order to get more detailed information about granulated materials microscopy of obtained materials was also conducted.

Table 2: Comparative characteristics of different series of granulated materials

№ composition	Indicators of technological properties			
	Bulk density, g/cm^3	flowability, g/sec	residual moisture, %	fractional composition
1	0,60	4,1	0,6	Fig. 2
2	0,55	3,2	0,8	Fig. 3
3	0,50	3,6	0,8	Fig. 4

From this we can conclude that all compositions of granulated materials (Table. 2) have good flowability and ready for the next stage of the process which is tableting. Below are pictures of sizes and shapes of granulated materials, as well as the results of sieving test.

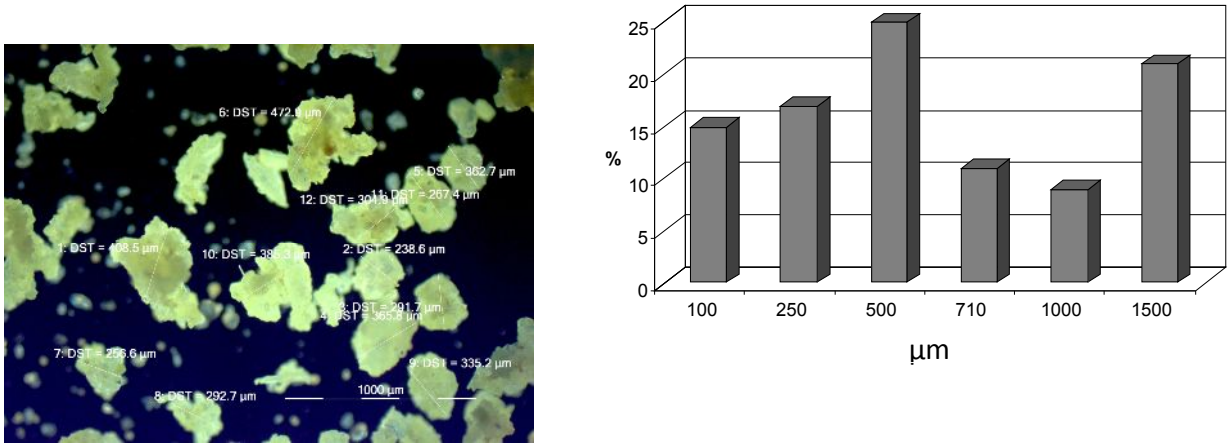

Figure 2: Results of microscopy and sieving test of granulated materials (composition 1)

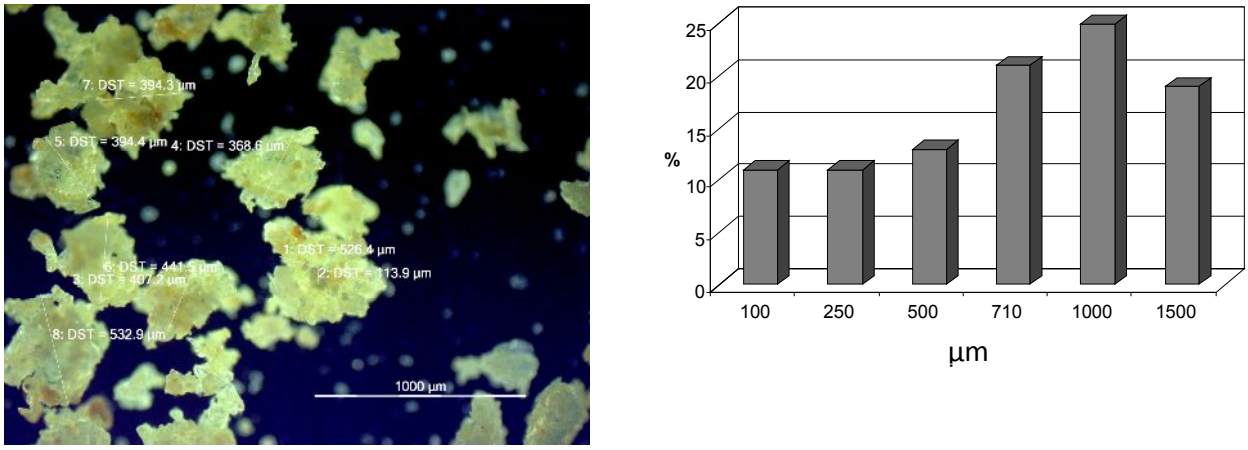

Figure 3: Results of microscopy and sieving test of granulated materials (composition 2)

Thus, three different compositions of granulated materials based on dry oat extract and quercetin obtained by wet granulation in a fluidized bed have pretty similar technological properties. Nevertheless we assumed and took for further investigation composition #3. Hence, microscopy of examination of granulated materials as well as sieving test data suggest that obtained mass may be subjected for tableting with the prospect of high-quality final product.

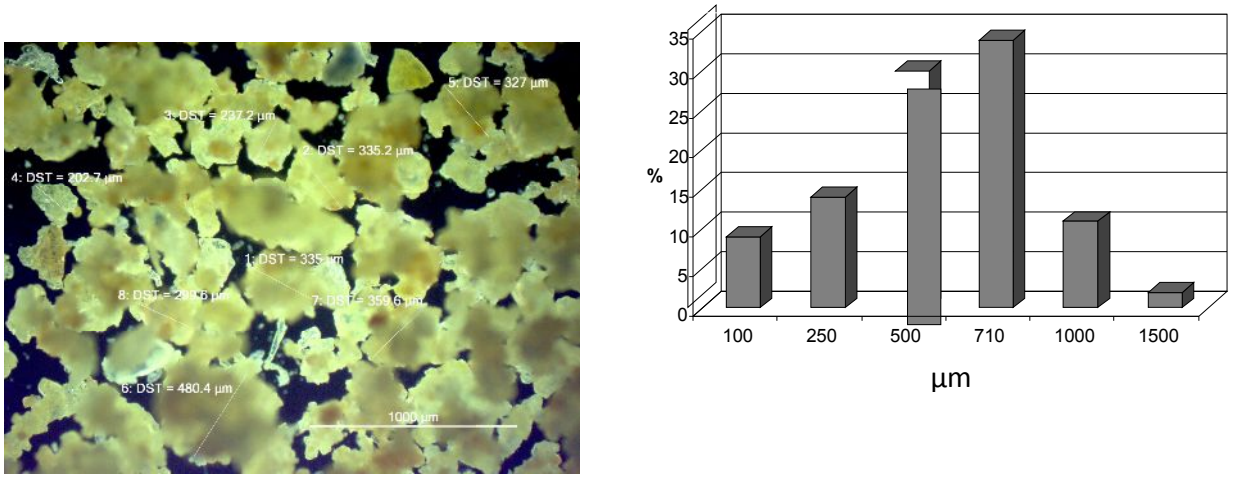

Figure 4: Results of microscopy and sieving test of granulated materials (composition 3)

Conclusion:

Three different compositions of granulated materials with similar technological properties were obtained by wet granulation method in a fluidized bed. It was experimentally confirm that wet granulation method in a fluidized bed could be used in order to obtain materials with good technological properties. Composition #3 was chosen as an optimal and the most interesting for further investigation. Obtained data allow us to proceed with further technological operation of tablet manufacturing which is tableting process.

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