Purification of the Synthesis Product of Salicylic Acid by means of Supercritical Carbon Dioxide

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Purification of salicylic acid synthesis product is carried out on fluid flow extraction device. Investigation of salicylic acid solubility on the isotherms 308 and 323 K in the range of pressures 9-33 MPa, and of phenol under temperatures of 308 K and 311 K was also conducted. The range of extragent flow rates was estimated, under which salicylic acid equilibrium concentration is reached in supercritical CO_2.

INTRODUCTION.

Salicylic acid is an important product of chemical pharmaceutical industry. Its derivatives and it itself have a wide application in food industry and medicine. Being an antiseptic and antioxidant it is used for tinned foods and for external use. Salicylic acid is used in dyestuff, synthetic fragrants production, in cosmetics. Its main usage is in aspirin production, which is a cooling medicine and analgetic.

Initial raw material for salicylic acid production is phenol. It is also the main contamination of salicylic acid synthesis product, moreover its main quantity is formed in the salicylic acid synthesis process as a result of side reaction. Thus obtained salicylic acid synthesis product contains about 99 % of o-Hydroxybenzoic acid calculated for dry substance.

During aspirin synthesis the quality of finite product is defined first of all by salicylic acid purity. That's why for chemical pharmaceutical preparations the technical salicylic acid after drying is cleaned by means of sublimation requiring great power expenditure. For this reason we made an attempt to clean the salicylic acid synthesis product by the method of supercritical fluid extraction using CO_2 as an extragent. For technical economical optimization of salicylic acid cleaning process and for estimations of technological process optimal parameters in industrial scale, our aim was to obtain data on pharmaceutical salicylic acid and main contaminations solubilities in supercritical CO_2 in a wide range of pressures and different temperatures.

MATERIALS AND METHODS

The research was conducted on constructed by us flow extraction device (Fig 1.) [1], with the possibility of polar co-solvent supply for the process of supercritical fluid extraction from solid matrix in the range of temperatures 305-363 K under the pressure 35 MPa. Before the beginning of the experiment CO_2 is pumped into the receiver (6) by membrane compressor (3). The initial sample in a special cartridge is placed into the extractor; all volumes and communications of device are washed by carbon dioxide under a small extra pressure, after that by means of a pressure reducer (7) in the extractor working pressure established, and liquid thermostating is started for maintaining process temperature. Pressures in the extractor and separator are measured by pressure gauges (29) and (30), the temperatures in characteristic points are measured by chromel-alumel thermocouples (T1-T4), introduced directly into the region of high pressure through the specially designed fittings.

For introducing of co-solvent into the gas flow a liquid syringe pump (16) with the cylinder of 150 ?m^3 is used. The pump performance is operated by electronic operating block (5). The introducing of co-solvent into the gas line is done between a pressure regulator (7) and a coil pipe heat exchanger of pre-heater (9). As the pressure regulator construction allows to work only with a gas phase, and the pump construction only with liquids, two reverse valves are installed in the system (28), preventing fluid penetration into the gas reducer and the gas into the pump. The syringe pump during one work cycle is able to pump approximately 100 g of organic co-solvent, which allows to obtain the mixture containing 1 ÷ 20 % mass of co-solvent. In pump working process the pressure, momentary flow rate and the volume of the cylinder fluid billing are constantly controlled.

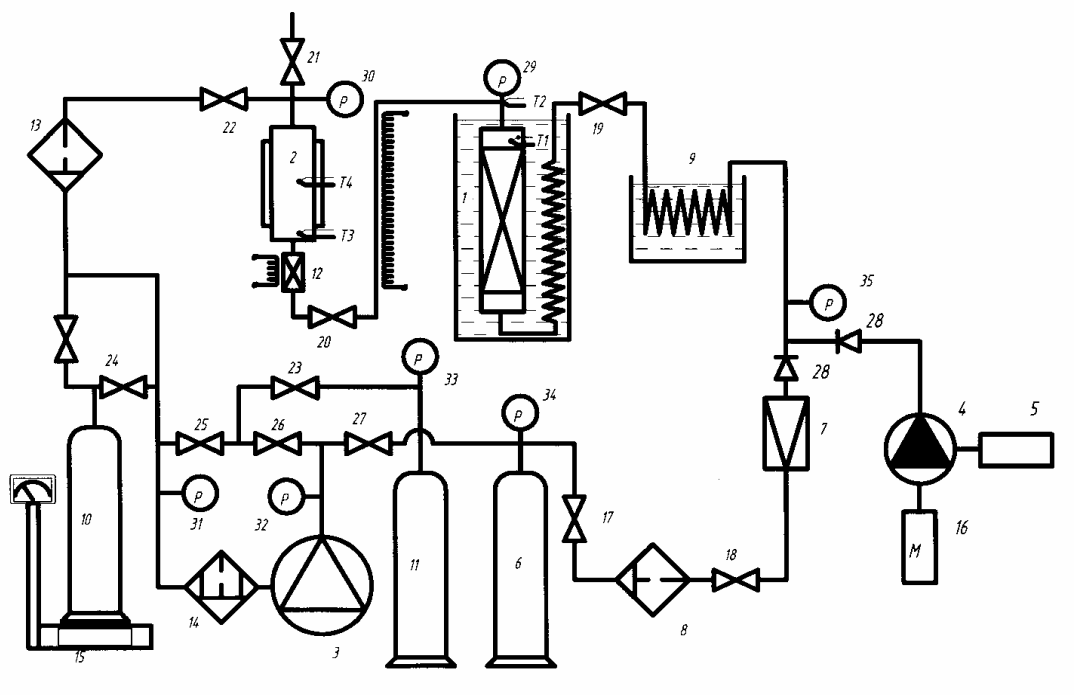

Figure 1. Schematic diagram of flow extraction apparatus.

The quantity of extragent let through the extracting material is estimated by weighing method. For this reason the cylinder (10) is put on the electron scales (15), which allows to define the weight of the cylinder before and after the extraction process with the accuracy of ± 0,025 kg. The quantity of the initial soluble and rafinate obtained after the extraction process is estimated by weighing on electron analytic scales with the accuracy of ± 10^{-5} kg.

For preventing the carrying away the salicylic acid synthesis product was pressed in tablets of 8 mm in diameter and 3 ÷ 3.5 mm high. The tablets pressing varied from 0.025 to 1.25 MPa for defining optimal parameters of the device work. Small pressing and flimsy tablets resulted in substantial carrying away of the substance from the extractor. High pressing resulted in reducing of dissolved substance mass due to reducing of tablets porous volume, which decreased the phase contact area in hard substance structure. It was established by means of the experiments that the optimal pressure of tablets pressing is 0.25÷0.30 MPa. Such pressure ensures sufficient strength and porosity of the tablets structure. During the investigation of pure components solubility for increasing the phase dividing surface, the tablets were reduced to fragments of 1.5÷3 mm.

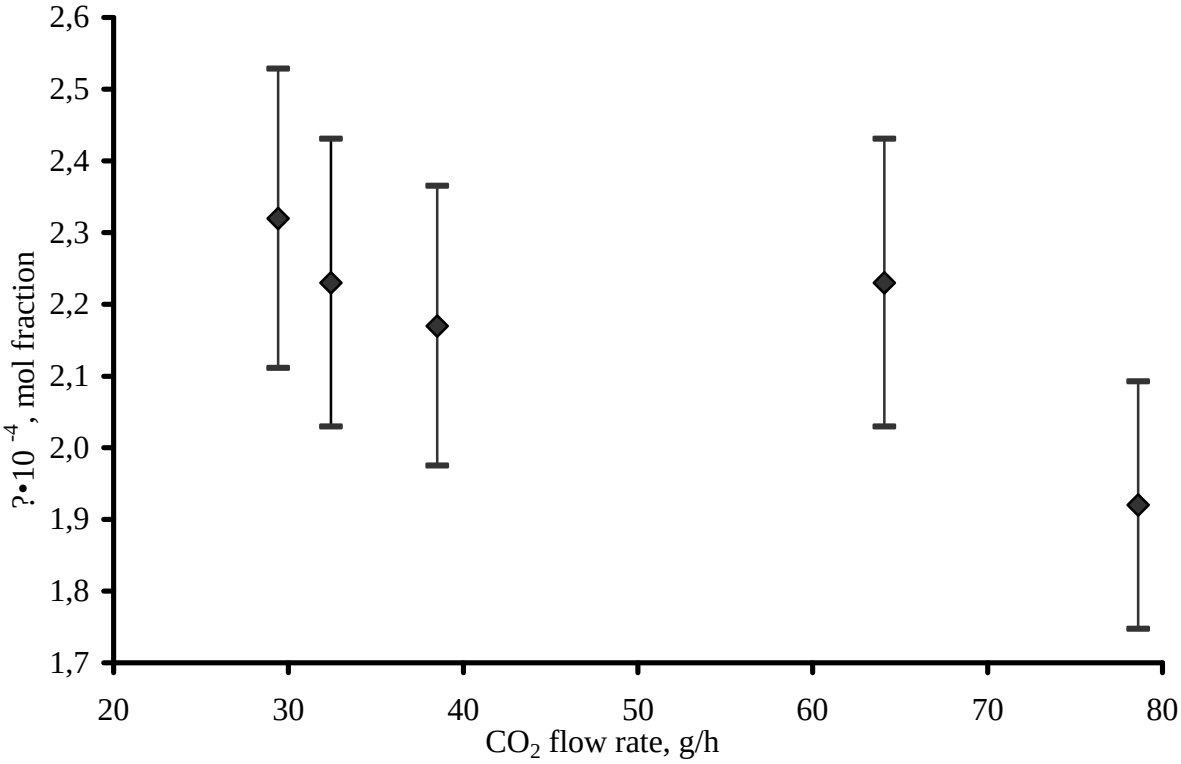

Figure 2. The influence of SC-CO2 flow rates on salicylic acid concentration.

To define the maximal extragent flow rate under which equilibrium concentration is achieved a series of experiments at the temperature of 311 K and pressure of 13.92 MPa was conducted. In all experiments initial samples of 9 ÷ 9.5 g were used, through which during the experiment 900 g of fluid were passed with different flow rates. Results of the experiments are shown on Fig. 2. The results of test experiments show that solubilities close to equilibrium are achieved at the flow rate of SC-CO_2 limited by 30÷50 g/h. For estimation of influence on the solubility of initial porous matrix at the same parameters an experiment was carried out with the salicylic acid powder loaded into the kapron cell at the fluid flow rate of 35 g/h. Obtained value of solubility agrees with the similar result for crushed tablets in the range of 1.5 %. It testifies the achievement of equilibrium concentrations of salicylic acid in supercritical carbon dioxide. In accordance with obtained data the measurements of solubility were carried out at the flow rate of SC-CO_2 in the range of 30÷50 g/h.

Such investigations for phenol were not conducted, because its solubility in supercritical carbon dioxide is two orders higher than that of salicylic acid, that's why it was accepted by us that in the chosen range of extragent flow rate the phenol equilibrium concentration will be achieved either.

CONCLUSION

In this work the principle possibility of purification of salicylic acid synthesis product by the method of supercritical fluid extraction was proved experimentally. Experiments were carried out at different pressures of extraction at 308 K. The quantity of the initial sample was 3.5÷4.5 g; the correlation between the hard sample quantity and the quantity of supercritical fluid was maintained constant for all the series if experiments being 1:200. The carbon

dioxide flow rate fluctuated during the experiments in the range of 0.03÷0.05 kg/h. The analysis results of rafinate are given in Table 1.

Table 1. results of salicylic acid synthesis product purification.

	Initial product of synthesis	Extraction pressure, MPa			
		7.8	9.4	10.8	12.0
Content of salicylic acid in rafinate, % mass.	99.21	100.00	100.00	99.95	99.85

It is evident from the results that in all cases after extractions the concentrating of salicylic acid in the initial product was observed, the degree of concentrating became less with the increase of extraction pressure. At the pressures lower than critical pressure of pure carbon dioxide (P_c=7.3 MPa) it is observed the sharp reduce of CO_2 capability for admixtures in the salicylic acid synthesis product. At pressures higher 7.8 MPa the solubility of above mentioned admixtures practically doesn't depend on pressure. For this reason the recommended pressure for the process of salicylic acid purification is 7.8 MPa, as more energetically profitable.

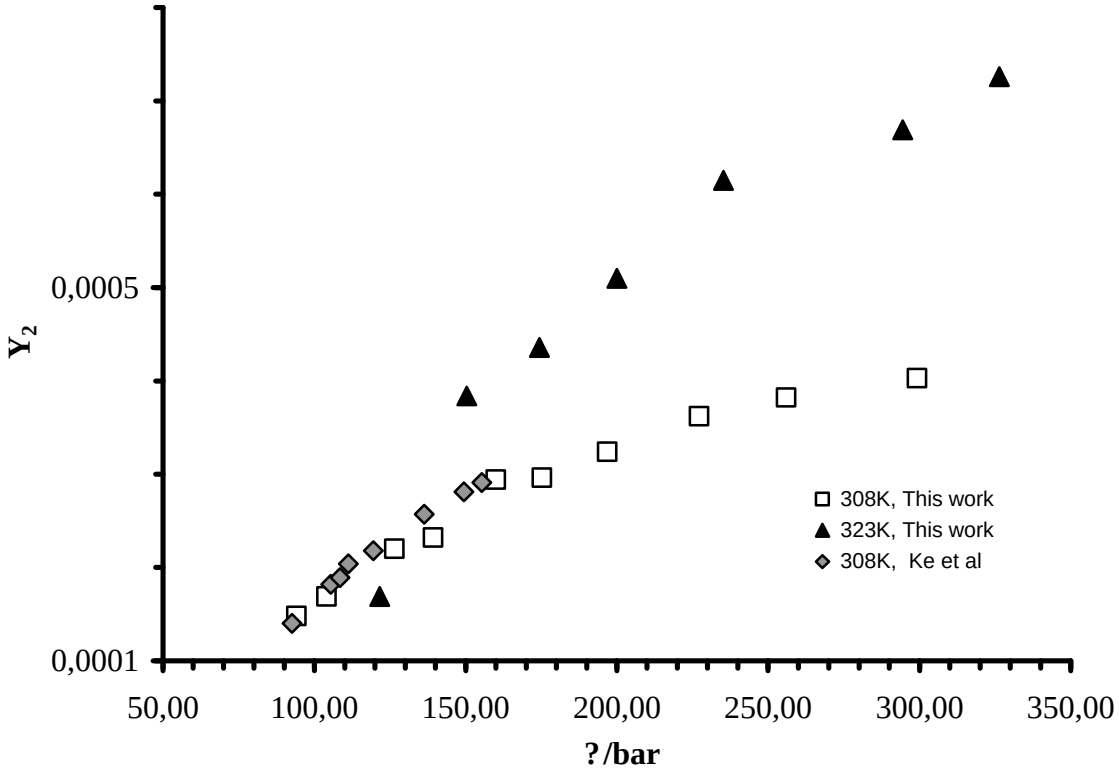

Figure 3. Salicylic acid solubility in supercritical CO_2

The measurements of pure salicylic acid solubility in supercritical carbon dioxide were carried out on isotherms 308 K and 323 K in the range of pressures from 9 to 33 MPa. These results are presented on Fig. 3, were the comparison of measurement results obtained on circular device with existing literature data [2] is also shown. At error of measurements estimated by us as 7.8 %, the given results agree with the results [2] in the range of 9 %.

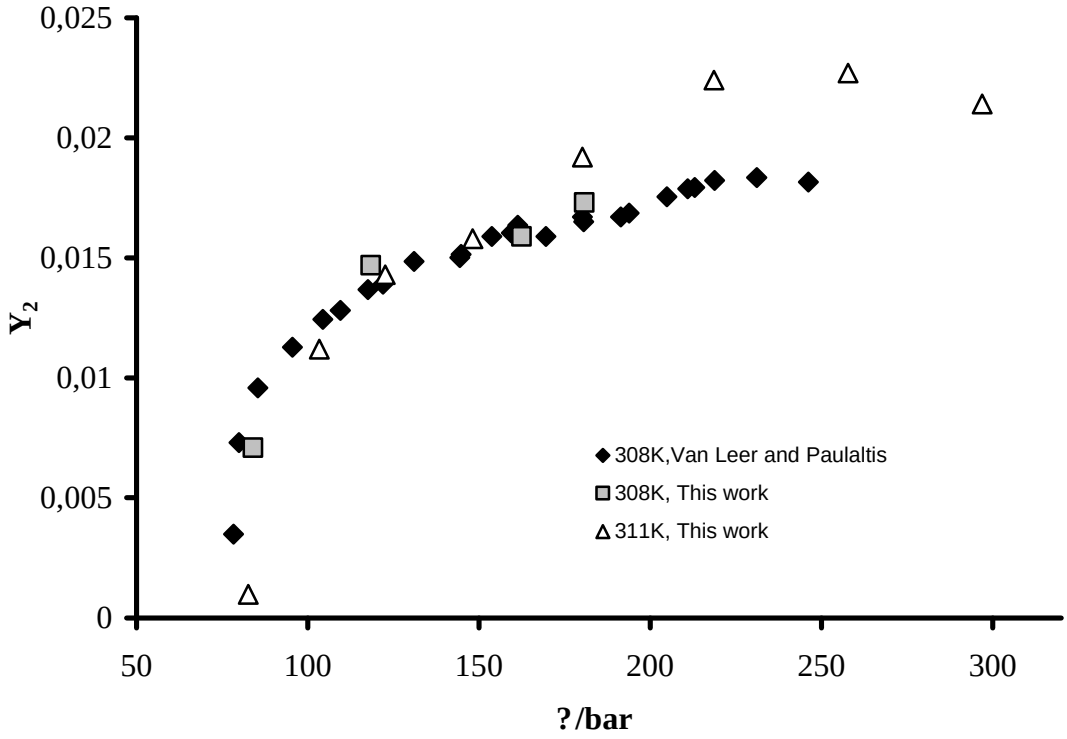

Figure 4. Phenol solubility in supercritical CO_2

The phenol solubility measurements are carried out at the temperature 308 K in the range of pressures from 8 to 20 MPa and at the temperature of 311 K in the range of pressures from 8 to 30 MPa. These results are presented on Fig. 4, where the comparison of measurement results with existing literature data [3] obtained on isotherms 308 K is also shown. For phenol, good agreement of results with literature data is observed. Maximal discrepancy with literature data makes 19.6 % for the dot lying in the region of sharp solubility growth (8.3 MPa) at the critical point of pure solvent, whereas for the rest dots it doesn't exceed 7 %.

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