

# The mechanochemically prepared compositions of skin care substances with silicates for medicinal and cosmetic applications

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## Keywords

biologically active substances; mechanical activation; neutralization reactions; silicates; solid organic acids

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## Abstract

**Introduction:** The active biological substances used in medicinal and cosmetic applications, are mainly organic acids. The local contact effect of the protons located on the surface of their crystallites can irritate the mucous membranes of the stomach and esophagus (medicines), or skin of the face (cosmetics). The irritating effect of protons can be weakened either by grinding crystalline acid powders to nanoscale sizes, or by neutralizing them. Organic acids are polymerized due to hydrogen bonds, which does not allow them to be dispersed to nanometric sizes by traditional methods. It was previously shown that during the mechanical activation of silicates, short-lived hydroxyl groups become available. **Objective:** The purpose of this work is to study the possibility of neutralization of protons of organic acids during their mechanochemical interaction with silicates. **Methods:** The IR spectroscopy, X-ray analysis and electron microscopy methods were used for research. **Results:** It was shown by that organic acid is "grafted" to the silicate surface due to neutralization of organic acid protons by hydroxyl groups of layered silicates, opened during mechanical activation. This makes it possible to form highly dispersed composite structures "organic acid/layered silicate" in dicarboxylic (carboxylic, aromatic, amino) acids - talc (pyrophyllite, kaolinite) systems. **Conclusions:** Such mechanochemically synthesized composites, in which acid is grafted to an inert carrier, in addition to high dispersion, provide a decrease in the acidity of the resulting product. In the case of mechanochemical interaction of SiO<sub>2</sub> with organic acids, the basic centers mainly work on the surface of SiO<sub>2</sub>, which is opened during mechanical activation. Organic acids (hydroxo acids, dicarboxylic, carboxylic, aromatic) are distributed in an extremely thin layer on the surface of silicon oxide due to the "SiO<sub>2</sub> — adsorption water — acid" bond. This allows to change the pharmacokinetics and avoid ulcerogenic action and reduce the irritating effect of organic acids on the skin.

## Introduction

Silicon dioxide and layered silicates are approved for use as inert pharmaceutical fillers in drug tableted forms [1,2]. In solid-phase cosmetics (especially in curative cosmetics), they are the basic compounds to produce powders, blushes, and eye shadows [3]. In such compositions fine particles obtained through preliminary grinding are in wide use. By this reason, the consumer properties of cosmetic products are strongly dependent on grinding quality.

The most frequently, active biological substances used in medicinal and cosmetic applications, are organic acids. The local contact effect of their crystallites protons can irritate the mucous membranes of the stomach and esophagus (medicines), or skin of the face (cosmetics).

Precursors for tablets, made from dispersed

particles of organic acids mixed with silicon dioxide and layered silicates, are often used in the production of pharmaceuticals and compact solid-phase cosmetics. Layered silicates and SiO<sub>2</sub> may be ground using traditional techniques. However, it is a great problem to comminute solid organic acids because of their structural features and the presence of hydrogen bonds. These bonds are readily broken under mechanical load but are rapidly recovered after the load is relieved. In this way, the crystal structures of acids and their individual properties are conserved during grinding. The problem may be solved by spreading the acid uniformly over the carrier surface. For the solid-phase components, it may be possible only in the case of the physicochemical interaction between the solid acid and the carrier, where the composite structures are formed as a result of *mechanochemical synthesis* [4]. During mechanical activation (MA), the native surfaces can form for a short time due to

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multiple shear deformations in particles, especially in layered silicates. These native surfaces undergo immediate relaxation, in particular, by interacting with pharmaceutical substances in accordance with the acid-base type of components. Thus, if a biologically active substance is mechanically activated with layered silicates, or silicon dioxide just before tableting, this can significantly modify the bioavailability of preparations, and probably improve the consumer qualities of curative cosmetics.

This assumption concerns both drug tablets based on solid organic acids already presented on the market, and curative cosmetic preparations in high demand. A similar approach has already demonstrated its high efficiency when the carriers of plant origin were used for drug delivery substances (arabinogalactan and dihydroquercetin) [5,6]. The present work is an attempt to generalize previous results on organic substances' mechanochemical interaction with silicate carriers, and to attract attention of the proposed approach to modify drugs in tablet form, and curative cosmetic preparations in order to enhance their efficiency.

## Experimental

In this research three types of silicate compounds were used:

- i) The nano sized silicon dioxide (with the particles smaller than 10 nm);
- ii) The dioctahedral kaolinite  $Al_2[Si_2O_5](OH)_4$ , which is the layered silicate of the 1:1 type;
- iii) The dioctahedral pyrophyllite  $Al_2[Si_4O_{10}](OH)_2$  with isomorphous silicates of 2:1 type,
- iv) The trioctahedral Mg-talc  $Mg_3[Si_4O_{10}](OH)_2$ .

The solid organic acids have been chosen as reagents to studying mechanochemical reactions with silicates: monocarboxylic stearic acid  $C_{17}H_{35}COOH$ ; lauric acid  $C_{11}H_{23}COOH$ ; dicarboxylic succinic acid  $(CH_2)_2(COOH)_2$ ; hydroxyl tetracarboxylic citric acid  $(CH_2COOH)_2C(OH)COOH$ ; aromatic benzoic acid  $C_6H_5COOH$  and hydroxy salicylic acid  $C_6H_4(OH)COOH$ ; and monoaminoacetic acid  $NH_2CH_2COOH$ .

The organic acids and their mixtures with layered silicates were mechanically activated in an AGO-2 planetary ball mill with water cooling, in the argon atmosphere. The drum volume was 250 cm<sup>3</sup>, balls diameter 5 mm, balls mass 200 g, the mass of samples under treatment was 10 g, and the rotation frequency of drums around the common axis was about 1,000 rpm [7]. IR absorption spectra were recorded with a Tensor-27 spectrometer, and the samples were prepared in accordance with the standard procedure of compacting with annealed KBr [8]. X-ray phase analysis was carried out with a D8 Advance (Bruker) diffractometer, using  $CuK\alpha$  radiation. Microphotographs were taken by a JEM-2000 FX-II transmission electron microscope.

## Results and discussion

The effect of MA on the crystal structures of silicates and solid organic acids in a high-energy planetary ball milling was studied earlier in our works [4, 9, 10]. It is known that the basic structural motif of kaolinite and talc is formed by networks of silicon-oxygen tetrahedra parallel to (001) planes. In kaolinite, these networks are packed as six - part cycles, and connected from one side with the 'gibbsite' layer, in which aluminum atoms are surrounded by four oxygen atoms each, and two OH groups to complete octahedra. The layers are held in between with hydrogen bonds [11, 12]. In talc, a layer is composed of two networks of  $SiO_4$ -tetrahedra, and one network of Mg-octahedra

which is located between them and bind them strongly. The IR spectra of silicon dioxide and layered silicates are well studied and interpreted [13-17]. The formation of paramagnetic centers of acidic and basic nature, which are able to react with surface  $SiO_3$  radicals, after MA in the inert atmosphere, was established in [18]. IR spectroscopic and X-ray structural studies of the talc and kaolinite MA showed that at initial stages, within the first 20 seconds, talc is only dispersed, while kaolinite exhibits noticeable structural distortions of tetra- and octahedral networks. During mechanical activation, as a result of M-OH bonds rupture and network destruction, acidic and basic surface centers are formed in crystal layers. Their recombination leads to the formation of water molecules. The lifetime of these centers is very short,  $10^{-7}$  -  $10^{-9}$  seconds [19]. The crystal structure of kaolinite and talc is completely destroyed after three-minutes, or more, of activation [9].

The solid organic acids dimerize and form cyclic pairs, with very strong hydrogen bonds between carbonyl and hydroxyl groups of two molecules [20]. The cyclic pairs of monocarboxylic acids are in contact with each other through the electrostatic interaction between oxygen atoms of hydroxyl groups, thus forming flat networks. Analysis of the IR spectra of acids before and after mechanical activation proves that their crystal structure is not distorted during this process, and depolymerization does not take place, because hydrogen bonds are not broken. It may be assumed that a network of monocarboxylic acids forms along sliding planes [21]. For this reason, the MA (which is shear strained along sliding planes) cannot lead to any substantial distortions in the network of strong hydrogen bonds. Interlayer bonds in acid packages are weak, and may be readily broken during activation, but they are rapidly restored after the load is removed. That is, interlayer bonds are broken during the MA, and protons may be available for chemical interaction with other substances within a very short time.

Previous IR spectroscopic studies [4,22] of products of mechanochemical reactions of layered silicate with monocarboxylic acids (stearic, palmitic, myristic, lauric, and benzoic) showed that, after the MA for thirty seconds to three minutes (depending on the acid nature), the intensity of the bands related to the vibrations of carboxyl groups in the acids decreases up to complete disappearance. The bands related to carboxylate ions and the bands of stretching and bending vibrations of water molecules appear, with a simultaneous decrease in the intensities of the bands of stretching and bending vibrations of hydroxyl groups in kaolinite. These changes in the IR spectra are likely to be the evidence of the solid-phase mechanochemical reaction, involving neutralization of hydroxyl groups in kaolinite by the protons of acids, resulting in the formation of a strong chemical bond between kaolinite and the acid. The IR spectrum of the formed product corresponds to the IR spectrum of the salt of carboxylic acid, within the range of characteristic frequencies. The IR spectra of the mixtures of kaolinite with stearic, palmitic, myristic, and lauric acids, reveal mainly a decrease in the intensity of the bands of stretching and bending vibrations of the surface OH groups. The bands of Si-O-Si and Si-O-(Al) lose their doublet nature [4,23].

A somewhat different situation is observed for amino acetic acid and its mixture with kaolinite. An amino acetic acid is organic compound with two different functional groups, acidic carboxyl group and amino group, which is basic. Therefore, amino acids may form salts both with bases and acids. According to [24], amino acetic acid has a layered crystal structure. Its molecules exist in the form of *zwitter* ions. They are bound with

each other through two relatively short, and, hence, rather strong hydrogen bonds  $N-H\cdots O$ , thus forming the layers parallel to the *ac* plane. The layers are composed of networks and are bound in pairs through weaker hydrogen bonds.

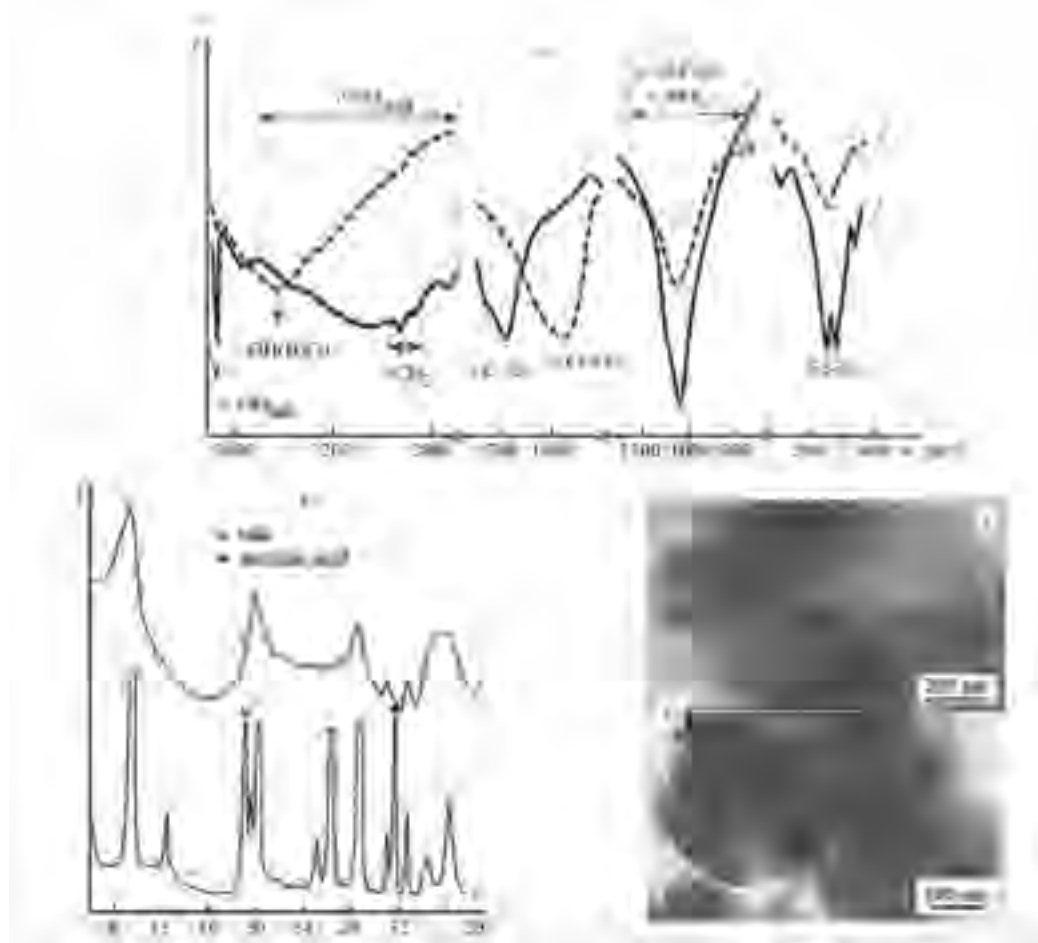
Analysis of the IR spectra of the mixtures of kaolinite with amino acetic acid, after 1 to 5 minutes activation, shows that the changes of the main bands related to kaolinite are almost the same as those in the spectra of activated pure kaolinite. After 1 minute MA, the bands, related to the stretching and bending vibrations of hydroxyl groups, disappear almost completely [16, 17]. At the same time, we observed a decrease in the intensity (until complete disappearance) of the bands related to the stretching and bending vibrations of NH groups, as well as the band related to the asymmetric stretching vibrations of  $COO^-$  in amino acetic acid. We may assume that the joint MA of kaolinite and amino acetic acid involves a solid-phase neutralization, resulting in the formation of a composite with the  $NH_2CH_2COO^-$  anion [10].

In [25,26], the interaction of piroxicam and meloxicam with aluminum oxide, during their joint mechanical treatment, was studied. It was demonstrated that the interaction proceeds due to the binding of the amide and sulfonamide groups of medicinal substances with the active centers on the surface of aluminum oxide and with the formation of the composites of a core-shell type. It was established by DRIFTS (Diffuse Reflectance Infrared Fourier Transform Spectroscopy), in the region of the stretching ( $\nu$ ) vibrations of OH groups and by NMR (protons)

[27], that the joint MA of indomethacin (IM) with  $SiO_2$  involves mechanochemical dehydration as a consequence of the chemical (acid-base) reaction between the  $SiO_2$  silanol groups and the IM carboxyl groups, with the formation of the IM/ $SiO_2$  mechanocomposite. According to NMR data, the joint MA is accompanied by a charge transfer and leads to the formation of a Si-O-C bridging bonds on the surface of the composite due to the following scheme:  $-COOH + -SiOH \rightarrow Si-O-C + H_2O$ . Also it leads to the interaction of IM methoxy and carbonyl groups with the induced free bonds on the  $SiO_2$  surface.

It may be assumed that basic short-living centers formed on the surface of layered silicates during their joint activation with organic acids may be neutralized by the protons of organic acids. In this case the layered silicate/anion composites of organic acid can be mechanochemically formed. Due to the neutralization of acid protons in these mechanocomposites, one may substantially increase the concentration of anions of organic acids, which are in fact the biologically active components of any medicinals, causing no irritation of the mucous membrane of the stomach, or the skin of face. The high dispersion ability of the composite's organic component enhances the biological availability.

Previously we have shown [4, 10] that the joint MA of silicates with monocarboxylic acids involved the neutralization of the protons of acids by hydroxyl groups of silicates. In those works, the mechanism of silicate interaction with dicarboxylic acids was studied.



**Figure 1.** IR spectra (a), X-ray diffraction patterns (b) and TEM images (c) of the talc + succinic acid mixture: initial (1) and after the MA for 3 minutes (2).

*T* — transmission,  $\nu$  — wavenumber ( $cm^{-1}$ ), *I* — intensity,  $2\theta$  — Bragg angle (deg); the same for Figs 2 – 10.

Dicarboxylic acids: succinic  $(\text{CH}_2)_2(\text{COOH})_2$ , glutaric  $(\text{CH}_2)_3(\text{COOH})_2$ , and suberic  $(\text{CH}_2)_6(\text{COOH})_2$  are characterized by layered crystal structures. They are polymeric [28] and form chains lying in one plane, with carboxyl groups bound each other in cyclic pairs by means of strong hydrogen bonds  $\text{OH}\cdots\text{O}$  [29]. In the crystal structure of glutaric acid, these chains form helices with  $\text{CH}_3$  groups in the inner space of the helices. Due to hydrogen bonds passing through a second-order axis, this structure is very rigid, so methyl groups cannot contact each other [21].

The molecules of suberic acid have an almost completely extended structure with hydrocarbon radicals packed in accordance with the type of orthorhombic lattice. They form infinite hydrogen-bound chains with the crystallographic inversion centers in the middle and at the ends of each molecule. These chains bound each other forming the corresponding infinite chains, with the help of hydrogen bonds where the OH groups participate both as donors and acceptors of protons. The fact that these chains are rather long determines the fatty acid nature [30].

Mechanochemical interactions of dicarboxylic acids with various layered silicates (talc, pyrophyllite, and kaolinite) were studied, taking succinic acid as an example.

#### Talc + succinic acid

After the talc + dicarboxylic succinic acid mixture taken at a mass ratio (m.r.) = 1:1, was mechanically activated for 3 minutes, the absorption bands related to the stretching vibrations  $\nu$  O-H in talc and the acid disappear from IR spectra almost completely, along with the  $\nu$  C=O band of acid dimers ( $1690\text{ cm}^{-1}$ ). The bands related to the carboxylate ion of succinic acid  $\nu_{\text{as}} 1590\text{ cm}^{-1}$ ,  $\nu_{\text{s}} 1440\text{ cm}^{-1}$  [20] and molecular water  $\nu$  OH( $\text{H}_2\text{O}$ )  $\sim 3430\text{ cm}^{-1}$  were observed [31] (Figure 1, a, curve 2). At the same time, the parameters of  $\nu$   $\text{SiO}_4^-$  bands and the bands of the  $\delta$  bending vibrations of the silicon – oxygen layer of talc were changed [32]. These data prove that the talc lattice deforms, and hydroxyl groups of talc are mechanochemically neutralized by the acid's protons. The product of the neutralization is the talc/acid anion mechanocomposite. The mechanochemical reaction of talc with succinic acid is participated in by not only the basic Mg–OH but also weakly acidic Si–OH groups of talc. According to the data reported in [33], Si–OH groups may act as basic ones if the pH of the medium is  $< 2$ . In this experiment, water

molecules formed and dissociated succinic acid ( $k_1 = 7.4 \times 10^{-5}$ ,  $k_2 = 4.5 \times 10^{-6}$ , respectively) create necessary conditions for the Si–OH groups of talc to participate in the mechanochemical neutralization. As a result, the formed composite is, in fact, the salt of succinic acid  $[\text{Mg}_3(\text{Si}_4\text{O}_{10})_2]^{+}(\text{COO}^-)_2(\text{CH}_2)_2$  [28]. Its IR spectrum does not contain the  $\nu$  bands of the OH groups of the silicate and acid's carboxyl groups (Figure 1a, curve 2). Changes in the parameters of the bands related to talc in the region below  $1100\text{ cm}^{-1}$  (Figure 1a) prove that talc lattice is deformed due to MA.

The x-ray diffraction patterns of the MA samples (Figure 1b) does not show the reflections of succinic acid. The reflections of talc are significantly broadened and shifted, but no more than 4% relative to the initial position of talc. The obtained data suggest that during the MA a mechanocomposite is formed, which “inherits” the type of the talc's crystal structure. This assumption is confirmed by high-resolution electron microscopy data, in accordance with which the talc/succinic acid composite is an agglomerate of lamellar particles, like the original talc (Figure 1c).

#### Pyrophyllite + succinic acid

Pyrophyllite is isomorphic to talc, but unlike the latter, it belongs to the 2:1 dioctahedral family, i.e., only two of three possible positions are occupied by  $\text{Al}^{3+}$  cations. During the MA of pyrophyllite with succinic acid (m. r. 1:1) for 3 minutes, similarly to the case of talc, the intensities of the  $\nu$  bands of the OH groups of the acid's silicate and the carboxyl groups decreased. The band  $\nu_{\text{as}}$  of carboxylate ion with the maximum at  $1595\text{ cm}^{-1}$  was observed. At the same time, changes of the parameters of  $\nu$  and  $\delta$  bands of  $\text{SiO}_4$  tetrahedron and the Si–O–Al and Si–O–(Al) bonds are observed (Figure 2, curve 2). These results prove the distortion of silicate lattice and the formation of mechanocomposite in accordance with the scheme similar to talc + succinic acid interaction. However, unlike for the activation of talc + succinic acid mixture, the IR spectrum of the pyrophyllite + acid mixture even after activation for seven minutes still contains a  $\nu$  C=O distinct band with the maximum at  $1710\text{ cm}^{-1}$ . At the same time, the  $\nu$  bands of OH groups, and Si–O–Al– and Si–O–(Al)-bonds of pyrophyllite disappear almost completely. The intensity of the  $\nu$  and  $\delta$  bands of  $\text{SiO}_4$  decreases, and the bands broaden. A broad band within the region of  $3700\text{--}2700\text{ cm}^{-1}$  becomes more intense (Figure 2, curve 3).

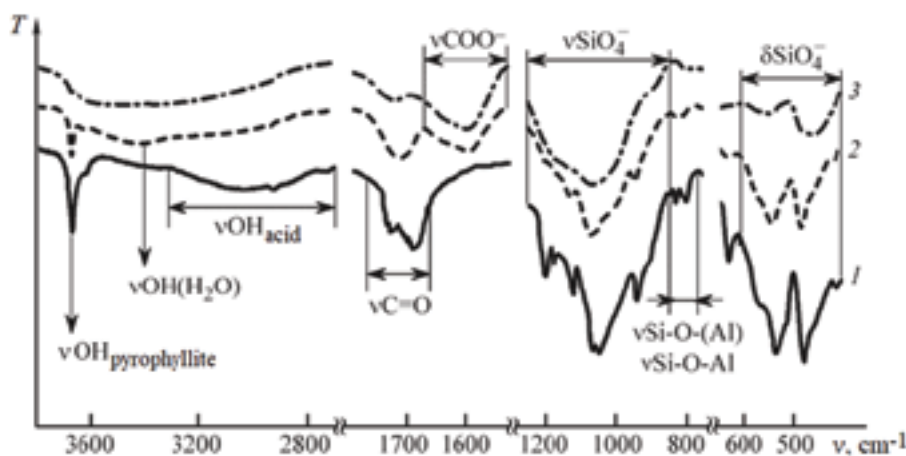


Figure 2. IR spectra of the pyrophyllite + succinic acid mixtures: initial (1) and after the MA for 3 (2) and 7 minutes (3).



The obtained data allow assuming that in the case of the MA of the pyrophyllite + succinic acid mixture, the mechanochemical neutralization of the basic active centers of the silicate takes place, not only with the acid's protons but also with the acid centers of the silicate itself. Indeed, only this is how we may explain the changes observed in the IR spectrum of the mixture after its activation for more than three minutes.

The difference in the mechanochemical interaction of succinic acid with isomorphous talc and pyrophyllite is due to the properties of cations in the octahedral network of silicates. In the structure of talc, all the three main cation positions of the network are occupied by  $Mg^{2+}$  ions, while in the pyrophyllite structure only two of three positions are occupied by  $Al^{3+}$  ions [13]. The position of Aluminum in the electrochemical activity scale is just to the right of magnesium. This enables assuming that the active centers of basic nature formed on the pyrophyllite surface, unlike for talc [34], are weaker bases than the anions of succinic acid. The possibility arises for the simultaneous neutralization of the basic centers of pyrophyllite by the acid centers of the silicate.

### Kaolinite + succinic acid

In the IR spectrum of the activated succinic acid + kaolinite mixture (Figure 3), similarly to the case of the acid with talc and pyrophyllite mixtures, when the MA duration increases, the intensities of the  $\nu C=O$  bands of the acid and the  $\nu OH$  bands of the acid and kaolinite becomes lower, the  $\nu SiO_4$  bands parameters of kaolinite change, and the  $\nu$  bands of OH groups of the molecular water are observed. When MA duration increasing, the diffraction patterns of the mixture show the decreased intensity and broadening of the kaolinite and succinic acid reflections. The obtained data state that, similarly to the mixtures considered above, mechanochemical interaction in the kaolinite + succinic acid mixture occurs, leading to the formation of kaolinite/acid anion composite. The IR spectrum of kaolinite + acid mixture activated for 7 minutes, similarly to the IR spectrum of pyrophyllite + succinic acid mixture, contains the acid bands  $\nu OH$ ,  $\nu C=O$  ( $1710\text{ cm}^{-1}$ ) and the composite bands  $\nu COO^-$ ,  $1590\text{ cm}^{-1}$  (Figure 3, curve 3). At the same time, the

spectrum does not contain the  $\nu OH$  bands of the silicate, while the  $\nu$ ,  $\delta SiO_4$  bands of the tetrahedron are broadened and do not contain clear maxima, which proves the distortion of the silicate structure. The broad asymmetric band with the maximum at  $\sim 3430\text{ cm}^{-1}$  is observed in the region of  $3800\text{--}2800\text{ cm}^{-1}$  in the spectrum of the kaolinite + acid mixture activated for 7 minutes, similarly to the case of pyrophyllite + acid mixture. It allows assuming that the MA of the kaolinite + acid mixture involves the mechanochemical neutralization of the basic active centers of the silicate not only with the acids' protons, but also by the active acid centers of the silicate. Taking into account the study on the capacity of layered silicates in reactions with organic acids, the resulting mechanocomposite can be represented as  $[Al_2(Si_2O_5)(OH)_3]^+ \cdot (COO^-)(COOH)(CH_2)_2$ .

The differences in the mechanochemical interaction of kaolinite and talc with succinic acid are due to the properties of cations in the octahedral networks and the structures of silicates. Kaolinite is a dioctahedral silicate of the 1:1 type and has four kinds of OH group. Unlike talc and pyrophyllite, both Al–OH and Si–OH groups of kaolinite are located not only on the side facets but on the basal (001) ones as well. The hydroxyl groups at the basal facets are almost lost their basic properties [33], and cannot take part in the mechanochemical silicate – acid neutralization.

It may be assumed that mechanochemical interaction proceeds in two stages: at the first, faster stage, within 1 minute, one of two carboxyl groups of each acid molecule participates in the process, and only then does the second COOH group enter the process. This stage of the process is much slower. It may also be assumed that a compound such as the acid salt of dicarboxylic acid is formed at the first stage of the process. To confirm this assumption, mixtures with different molar ratios of kaolinite to acid were considered. It follows from the analysis of IR spectroscopic data that a twofold decrease in the molar ratio reduces the reaction time in the system. An increase in the molar ratio of kaolinite to acid (1:0.5) causes the twofold increase in the reaction time. The nature of changes in the system remains the same.

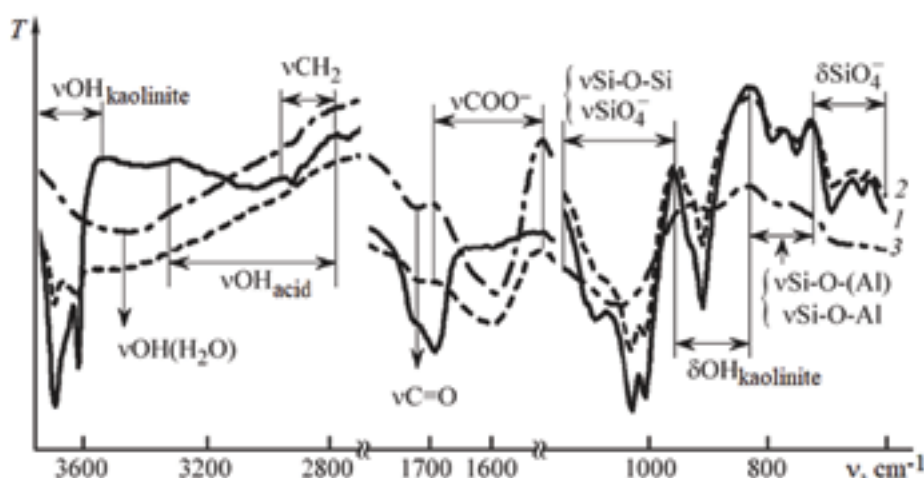


Figure 3. IR spectra of the kaolinite + succinic acid mixtures: initial (1) and after the MA for 3 (2) and 7 minutes (3).

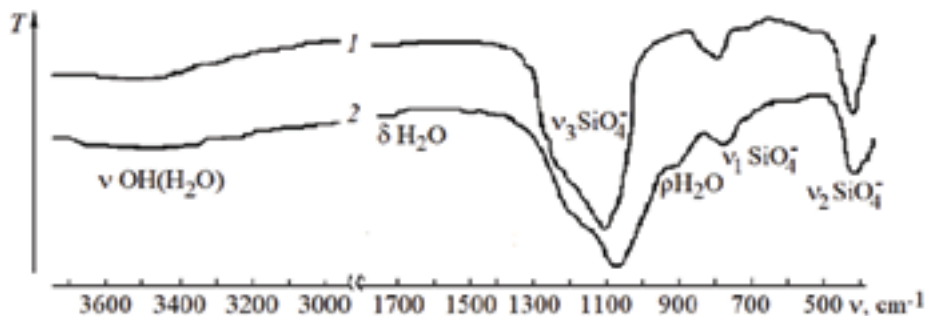


Figure 4. IR spectra of  $\text{SiO}_2$  before (1) and after the MA for 5 minutes (2).

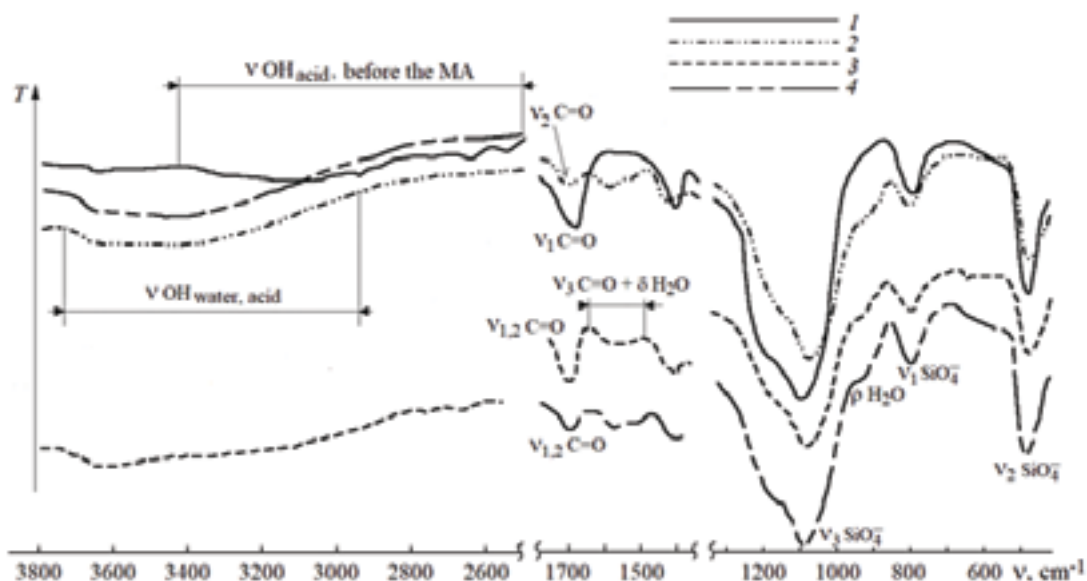


Figure 5. IR spectra of the  $\text{SiO}_2$  + succinic acid mixtures before (1) and after the MA for 3 (2), 5 minutes (3), 5 minutes + 0.5 mL  $\text{H}_2\text{O}$  (4). The m. r.  $\text{SiO}_2$ :acid = 20:1 (1, 2) and 6:1 (3, 4)

Mechanochemical interaction of organic substances containing various functional groups with aluminium and silicon oxides was studied in [25, 26]. It is shown that bridging Si-O-Si bonds are formed on the surface of composites.

It was demonstrated previously that silicon dioxide is a promising carrier for composite biopreparations [19,27,35,36]. The interaction of solid organic acids with silicon dioxide was studied. The IR spectrum of initial  $\text{SiO}_2$  was described in [16].

The clear bands in the spectrum of initial  $\text{SiO}_2$  (Figure 4, curve 1) with the maxima at 1100, 800, and 470  $\text{cm}^{-1}$  relate as follows: the first two bands – to the stretching vibrations ( $\nu_3, \nu_1$ ), the third band – to the bending ( $\nu_2$ ) vibrations of  $\text{SiO}_4$  tetrahedra [16,37]. Weak bands, a broad one with the maximum at ~3430-3440  $\text{cm}^{-1}$  –  $\nu$  OH ( $\text{H}_2\text{O}$ ) and another one with the maximum at 1640  $\text{cm}^{-1}$  –  $\delta$  ( $\text{H}_2\text{O}$ ) [32, 38] in the IR spectrum of  $\text{SiO}_2$  prove the presence of adsorbed water. After the 5 minutes of MA (Figure 4, curve 2), the  $\nu$  OH ( $\text{H}_2\text{O}$ ) band becomes asymmetric and broaden. At the same time, the maximum of the  $\nu_3$  band (O–Si–O, Si–O–Si vibrations) of  $\text{SiO}_4$  tetrahedra shifts to lower frequencies: 1100  $\text{cm}^{-1}$   $\rightarrow$  1080  $\text{cm}^{-1}$ . A shoulder can be seen at this band in the region of 950-850  $\text{cm}^{-1}$ . The band related to the bending vibrations also shifts from 470  $\text{cm}^{-1}$  to 460  $\text{cm}^{-1}$ .

The obtained data prove definite distortions of the  $\text{SiO}_2$

structure during the MA and allow us to assume that active centers are formed on the surface of the  $\text{SiO}_2$  samples due to distortions of their structure as a result of a longer than 1 minute MA [18]. According to the data reported in [19], the active centers of the mechanically activated  $\text{SiO}_2$  are mainly acidic, and only some of them are basic. These basic centers are likely to interact with molecules of adsorbed water through hydrogen bonds. The shoulder at the  $\nu_3$   $\text{SiO}_4^-$  band in the spectra of activated samples within the region 950-850  $\text{cm}^{-1}$  confirms this. The shoulder is related to the  $\rho$   $\text{H}_2\text{O}$  rocking vibrations [31, 32, 38] of water molecules bound with  $\text{SiO}_2$ . At the same time, the shape and positions of the maxima of the  $\nu$  and  $\delta$  bands of OH( $\text{H}_2\text{O}$ ) change (Figure 4, curve 2).

#### $\text{SiO}_2$ + succinic acid

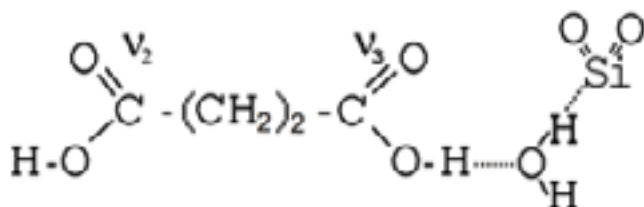
In the IR spectrum of the  $\text{SiO}_2$  + succinic acid mixture at a mass ratio  $\text{SiO}_2$ :acid = 20:1 activated for 3 minutes (Figure 5, curve 2), two bands are observed. One of them is seen with the maximum at 1725  $\text{cm}^{-1}$ , and another is broad, with maxima at ~1600 and 1550  $\text{cm}^{-1}$ , instead of the  $\nu_1$  band of stretching vibrations of carbonyl groups C=O of the dimers of initial acid, with the maximum at 1685  $\text{cm}^{-1}$ .

At the same time, the band with the maximum at 1420  $\text{cm}^{-1}$  [ $\nu$  C-O- +  $\delta$  OH (COOH)] [20, 29] broadens substantially. Its

maximum becomes less clear and shifts to  $\sim 1445\text{ cm}^{-1}$ . We also observed that the  $\nu\text{ OH}$  band disappeared in the region of  $3400\text{--}2500\text{ cm}^{-1}$ , characteristic for the dimer acid molecules [20, 29]. A broad diffuse band at  $\sim 3750\text{--}2800\text{ cm}^{-1}$  in the region of the stretching vibrations of OH groups is observed in the IR spectrum of the mixture after the MA.

Changes of the  $\text{SiO}_2$  characteristic bands are similar to those in the IR spectra of  $\text{SiO}_2$  activated for more than 1 minute (Figures 4 and 5, curves 2). A band is seen in the region of  $950\text{--}850\text{ cm}^{-1}$  as well.

The obtained data allow assuming that the MA of the mixture involves the rupture of bonds in the acid's associates. The acid mono-molecules interact through hydrogen bonds with water molecules, while the latter are, in turn, bound through hydrogen bonds with active centers on the  $\text{SiO}_2$  surface. The proposed scheme of the  $\text{SiO}_2$  interaction with acid can be expressed as follows:



**Scheme 1.** Interaction of  $\text{SiO}_2$  with succinic acid

According to the scheme 1, the band with the maximum at  $1725\text{ cm}^{-1}$  (Figure 5, curve 2) should be attributed to the  $\nu_2\text{ C=O}$  vibrations of monomeric acid molecules, while a broad band with weakly expressed maxima at  $1600$  and  $1550\text{ cm}^{-1}$  relates to the  $\delta\text{ H}_2\text{O} + \nu_3\text{ C=O}$  vibrations, and  $\nu_1\text{ C=O}$  relates to the initial dimeric acid molecules. The band related to the  $\nu\text{ C-O}$  vibrations, as expected [20], shifts in the opposite direction with respect to the shift of the  $\nu\text{ C=O}$  band, that is,  $1420\text{ cm}^{-1} \rightarrow 1445\text{ cm}^{-1}$  (Figure 5, curve 2). A broad diffuse band in the region of  $3750\text{--}2800\text{ cm}^{-1}$  relates to the stretching vibrations of OH groups, the  $\nu\text{ OH}$  vibrations of the monomeric acid molecules, and water molecules held by hydrogen bonds (Figure 5, curve 2; Scheme 1). Taking into account the shift of the  $\nu\text{ C=O}$  vibration band, one may suppose that hydrogen bonds formed between

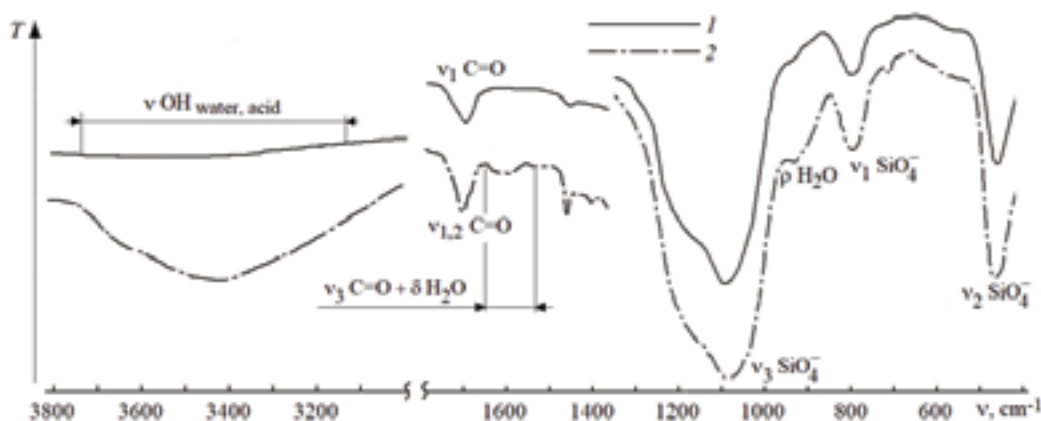
water molecules and monomeric acid molecules are rather strong. It should be noted that the bands related to dimeric acid molecules are still present in the IR spectra of the  $\text{SiO}_2 +$  succinic acid mixtures at the mass ratio  $< 20:1$  after 5 minutes or more of the MA. For instance, for the mass ratio of  $6:1$ , the  $\nu_2\text{ C=O}$  band of monomeric acid is asymmetric with maximum not at  $1725\text{ cm}^{-1}$  but at  $1720\text{ cm}^{-1}$ , and a shoulder at  $\sim 1700\text{ cm}^{-1}$  due to the vibrations of  $\text{C=O}$  groups in dimeric acid molecules,  $\nu_1\text{ C=O}$  (Figure 5, curve 3). In the region of stretching vibrations of OH groups,  $3000\text{--}2500\text{ cm}^{-1}$ , there are weak but clear maxima characteristics of  $\nu\text{ OH}$  dimeric molecules of succinic acid. We suppose that the bands related to dimeric molecules in the IR spectra prove the lack of basic active centers on the  $\text{SiO}_2$  surface to bind more acid molecules. If water (in the amount of  $0.5\text{ mL}$ ) is added to the mixture of  $\text{SiO}_2 +$  succinic acid with the mass ratio of  $6:1$ , it does not change the case. The bands related to acid dimer molecules are still observed in the IR spectra of the MA product. These results further confirm our assumption that only basic  $\text{SiO}_2$  surface centers take part in mechanochemical interaction with succinic acid. The reaction proceeds completely under the condition that the mass ratio of  $\text{SiO}_2$  and succinic acid should be  $> 6:1$ .

### $\text{SiO}_2 +$ monocarboxylic acids

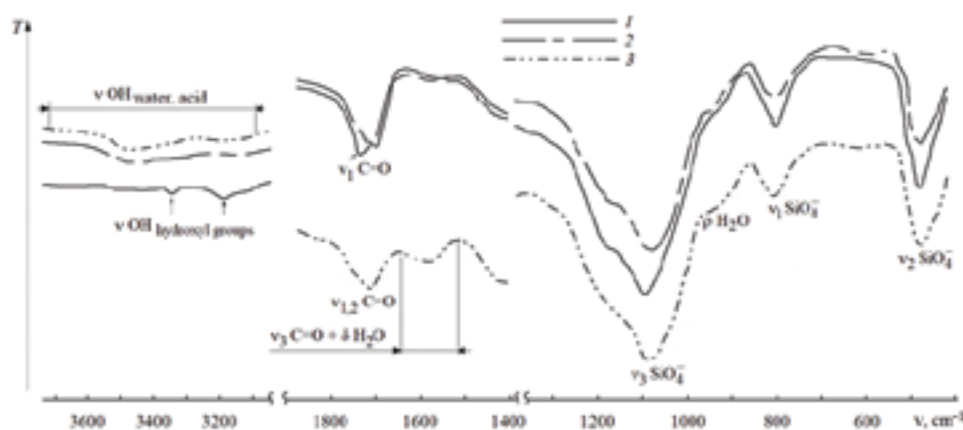
The interaction during the joint activation of  $\text{SiO}_2$  with the saturated monocarboxylic acids, stearic (HSt), and lauric (HL) proceeds in a similar manner. The hydrogen bonds of monomeric acid molecules with the molecules of adsorbed water (due to Scheme 1) are likely to be weaker than in the case of succinic acid.

Indeed, in the IR spectrum of the activated HSt +  $\text{SiO}_2$  mixture, a broad band ( $\delta\text{ H}_2\text{O} + \nu_3\text{ C=O}$ ) is shifted to higher frequencies to  $1620\text{--}1590\text{ cm}^{-1}$ , while the  $\nu_3\text{ SiO}_4^-$  band has its maximum at  $1085\text{ cm}^{-1}$ . In the IR spectrum of the MA product of  $\text{SiO}_2 +$  stearic acid mixture,  $\nu_3\text{ SiO}_4^-$  has its maximum at  $1070\text{ cm}^{-1}$ , while the maxima of the overall band ( $\delta\text{ H}_2\text{O} + \nu_3\text{ C=O}$ ) are observed at  $1600$  and  $1550\text{ cm}^{-1}$ .

The participation of adsorbed water in the mechanochemical interaction of  $\text{SiO}_2$  with mono- and polycarboxylic saturated acids (Scheme 1) proves that the IR spectra of the composites formed during the MA remain unchanged after exposure at  $T = 155\text{--}160\text{ }^\circ\text{C}$  for 3 hours.



**Figure 6.** IR spectra of the  $\text{SiO}_2 +$  stearic acid mixtures before (1) and after the MA for 9 minutes (2). The *m. r.*  $\text{SiO}_2\text{:acid} = 20:1$

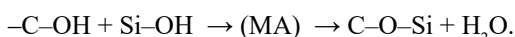


**Figure 7.** IR spectra of the  $\text{SiO}_2$  + citric acid mixtures after the MA for 30 seconds (1), 3 (2) and 5 minutes (3). Mass ratio  $\text{SiO}_2$ :acid = 3:1.

### $\text{SiO}_2$ + hydroxy acids

The  $\text{SiO}_2$  + tricarboxylic hydroxy acid (e.g. citric) mixture MA also leads to the formation of a chemical bond between the components. In the IR spectra of the activated  $\text{SiO}_2$  + citric acid mixture, we observe changes in the bands of silicon dioxide and the acid (Figure 7). The bands of the OH stretching vibrations in carboxyl and hydroxyl groups at  $3700\text{--}2900\text{ cm}^{-1}$  are not observed; bands with the maximum at  $1725\text{ cm}^{-1}$  are seen –  $\nu_2\text{ C=O}$ , as well as the bands within the regions of  $1650\text{--}1550\text{ cm}^{-1}$  – ( $\delta\text{ H}_2\text{O} + \nu_3\text{ C=O}$ ) and  $950\text{--}850\text{ cm}^{-1}$  –  $\rho\text{ H}_2\text{O}$ . In the IR spectra of the non-activated mixture, the  $\nu_1\text{ C=O}$  band of citric acid has two maxima:  $1710\text{ cm}^{-1}$  and  $1750\text{ cm}^{-1}$ , related to the  $\nu\text{ C=O}$  vibrations of the acid's associates and  $\nu\text{ C=O}$  of the carboxyl groups respectively, that do not participate in the formation of associates.

The data obtained allow it to be assumed that not only the OH of the carboxyl groups take part in the mechanochemical interaction in the  $\text{SiO}_2$  + citric acid system but also the acid's hydroxyl groups interacting with the acid centers on the  $\text{SiO}_2$  surface [19]. As a result, a bridge bonds between the carrier and the acid and water are formed [19,27]:



Citric acid may interact with  $\text{SiO}_2$  mechanochemically if the m. r.  $\text{SiO}_2$ :acid = 3:1, which is likely to be due to the possible participation of the acid's hydroxyl groups in this interaction.

### $\text{SiO}_2$ + aromatic acids

#### Monocarboxylic acids

In the IR spectra of the activated  $\text{SiO}_2$  + benzoic acid mixtures, m. r. = 20:1 (Figure 8), changes of the parameters of the bands related to the vibrations of  $\text{SiO}_4^-$  tetrahedra of silicon dioxide are similar to the changes in the IR spectra of the above considered mixtures (Figures 5–7). The  $\rho\text{ H}_2\text{O}$  band appears at  $950\text{--}850\text{ cm}^{-1}$ ; the  $\nu_1\text{ C=O}$  band broadens substantially, becomes asymmetric.

Changes are also observed in the absorption within the regions  $3750\text{--}2400\text{ cm}^{-1}$  –  $\nu\text{ OH}$  vibrations in water and benzoic acid, and  $1700\text{--}1400\text{ cm}^{-1}$ . However, these changes are less clear, maybe due to five bands of in-plane  $\nu\text{ C=C}$  skeletal vibrations in the region of  $1650\text{--}1430\text{ cm}^{-1}$  [20,29]. One of these bands is shifted to lower frequencies,  $1585 \rightarrow 1560\text{ cm}^{-1}$ , because the position of the band depends on the type of substituents. These

facts, in particular the shift of one of the  $\nu\text{ C=C}$  bands, may be the evidence of the mechanochemical interaction of  $\text{SiO}_2$  with benzoic acid during their joint MA.

#### Aromatic hydroxy acids

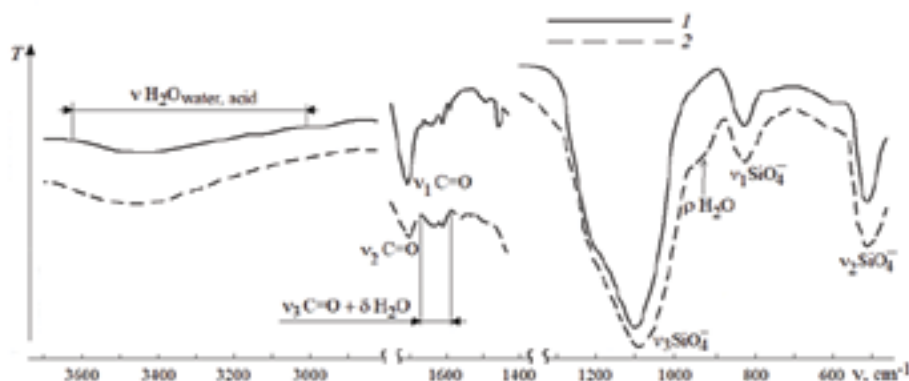
Mechanochemical interaction of  $\text{SiO}_2$  with salicylic acid differs significantly from its interaction with benzoic acid because aromatic hydroxy acids may exhibit chemical properties of both monocarboxylic acids and monohydric monatomic alcohols.

It follows from the analysis of the IR spectra (Figure 9) that after 1 minute MA of a salicylic acid +  $\text{SiO}_2$  mixture (m. r. = 14:1), the intensity of the band at  $1665\text{ cm}^{-1}$ ,  $\nu_1\text{ C=O}$  of the acid's carboxyl groups, decreases substantially. The band is broaden, and its maximum becomes diffuse. Within the region of  $1650\text{--}1550\text{ cm}^{-1}$ , instead of a  $\nu\text{ C=C}$  narrow band,  $1615\text{ cm}^{-1}$  [20, 29], a broad band is observed, with two maxima:  $\sim 1615\text{ cm}^{-1}$  and  $1595\text{ cm}^{-1}$  (more clear).

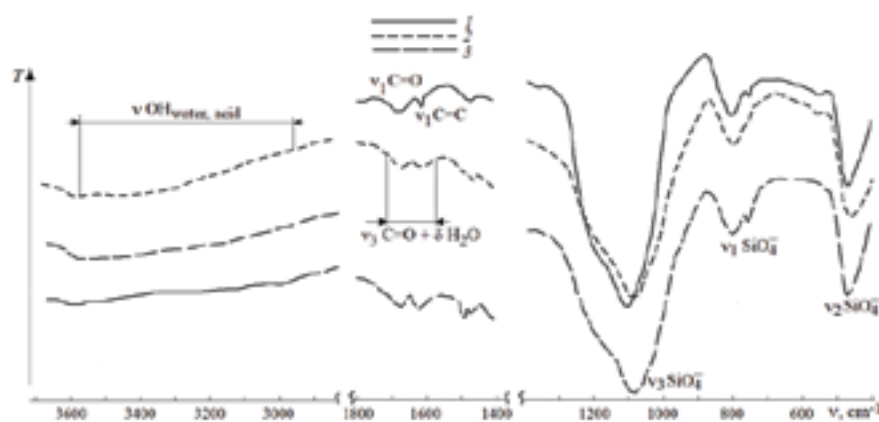
Similarly to the mixtures of the  $\text{SiO}_2$  with mono- and polycarboxylic acids, a shift of the  $\nu_1$ ,  $\nu_2$ ,  $\nu_3$  bands of  $\text{SiO}_4^-$  tetrahedra in  $\text{SiO}_2$  is observed in the IR spectrum of this mixture. However, unlike for the examples considered above, the  $\rho\text{ H}_2\text{O}$  band in the form of a shoulder of the  $\nu_3\text{ SiO}_4^-$  band, in the region  $850\text{--}950\text{ cm}^{-1}$ , can hardly be visible (Figure 9). For this reason, taking into account the features of the chemical properties of aromatic hydroxy acids, one may assume that the mechanochemical interaction with  $\text{SiO}_2$  is participated both by the carboxyl groups and phenolic hydroxyls of salicylic acid.

Phenolic (alcoholic) hydroxyl groups of the acids, similarly to hydroxyl groups of hydroxy acids, interact mechanochemically with the acid centers of the  $\text{SiO}_2$  surface to form water. The acidic carboxyl groups interact with  $\text{SiO}_2$  during the MA similarly to the case of mono- and polycarboxylic acids (Scheme 1), that is, through hydrogen bonds between hydroxyl fragments of the carboxyl groups in monomeric acid molecules and water molecules, which are, in turn, bound through rather strong hydrogen bonds with the basic centers on the  $\text{SiO}_2$  surface. The position of the maximum of  $\nu\text{ C=C}$  band ( $1615\text{ cm}^{-1}$ ) in the IR spectra of aromatic compounds depends on the presence and nature of substituents [19,28]. For this reason, in the IR spectrum of the product of the MA of a  $\text{SiO}_2$  + salicylic acid mixture the maximum of the  $\nu\text{ C=C}$  band shifts to lower frequencies:  $1615\text{ cm}^{-1} \rightarrow 1595\text{ cm}^{-1}$ .





**Figure 8.** IR spectra of the  $\text{SiO}_2$  + benzoic acid mixtures before (1) and after MA for 3 minutes (2). m. r.  $\text{SiO}_2$ :acid = 20:1



**Figure 9.** IR spectra of the  $\text{SiO}_2$  + salicylic acid mixtures before (1) and after the MA for 3 (2) and 5 minutes (3); m. r.  $\text{SiO}_2$ :acid = 14:1 (1, 2) and 7.5:1 (3)

### $\text{SiO}_2$ + amino acetic acid

Changes in the characteristic bands of  $\text{SiO}_2$  in the IR spectra of the activated  $\text{SiO}_2$  + amino acetic acid mixtures are similar to those in the IR spectra of all the above-considered activated systems. For instance, in the mixture of  $\text{SiO}_2$  with amino acetic acid at a mass ratio of 8:1 (Figure 10) after activation for 3 minutes, the bands characteristic of stretching and bending vibrations of  $\text{NH}_3^+$  groups are not observed within the regions 3400–2300, 2200–2050 and 1550–1450  $\text{cm}^{-1}$ , respectively, as well as the  $\nu_{\text{as}} \text{COO}^-$  band 1700–1550  $\text{cm}^{-1}$  [20, 29].

Instead of the indicated bands, new bands are observed: a broad diffuse band with scarcely noticeable maxima at 3650 and 3250  $\text{cm}^{-1}$  in the region of 3700–2700  $\text{cm}^{-1}$ , and a broad band with the maximum at 1635  $\text{cm}^{-1}$ . However, unlike for the IR spectra of the activated  $\text{SiO}_2$  + aromatic acids mixtures, in this case, the band related to the out-of-plane  $\rho \text{H}_2\text{O}$  rocking vibrations of bound water is practically invisible (the region of 950–850  $\text{cm}^{-1}$ , Figure 10).

Similar changes of the bands related to the vibrations of  $\text{NH}_3^+$  and  $\text{COO}^-$  groups of amino acids were observed during the study of the MA of leucine with talc [39] and phenylalanine with kaolinite, talc,  $\text{SiO}_2$  and  $\alpha$ -,  $\gamma$ - $\text{Al}_2\text{O}_3$  [19]. They assumed that leucine and phenylalanine in the products of activation are present as  $\text{NH}_2\text{CHR}\text{COO}^-$ , with both nitrogen and oxygen atoms bound to the carrier. Basing on these considerations, and taking into account that the  $\rho \text{H}_2\text{O}$  band related to water bound

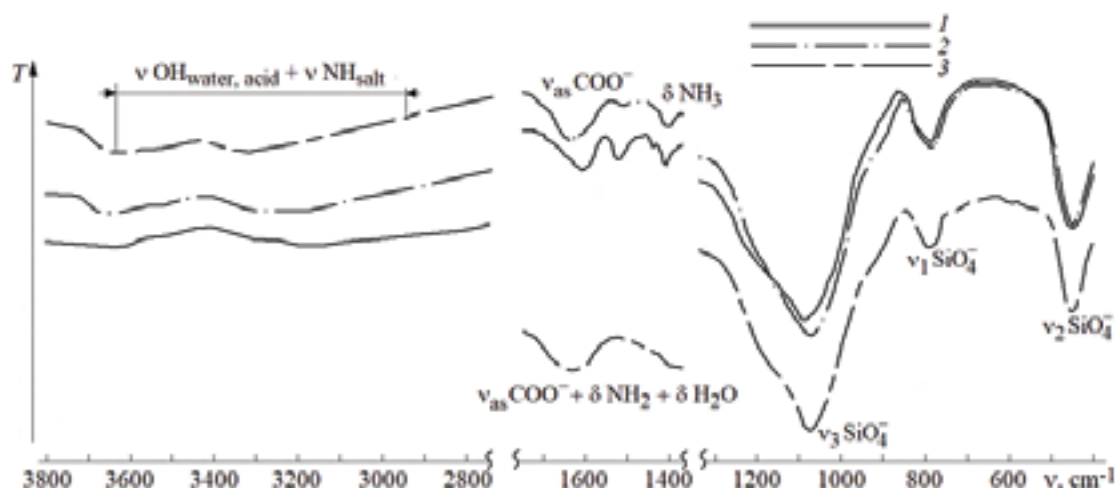
to silicon dioxide is almost not seen in the IR spectra of the  $\text{SiO}_2$  + amino acetic acid activated mixtures, we suppose that the interaction of  $\text{SiO}_2$  with amino acetic acid proceeds without participation of water molecules. In the composite material formed, the acid's amino groups interact with the basic centers on the carrier's surface, while the carboxyl groups interact with its acid centers.

In the IR spectrum of the amino acetic acid +  $\text{SiO}_2$  mixture after the MA, the band in the region of 3700–2700  $\text{cm}^{-1}$  relates to the stretching vibrations of  $\text{NH}_2$  groups and water molecules, possibly bound with the anion of amino acetic acid and  $\text{SiO}_2$  [20,32,39].

The band with the maximum at 1635  $\text{cm}^{-1}$  should be attributed to several vibrations: asymmetric stretching vibrations of  $\text{COO}^-$  groups of amino acetic acid [20,29], water molecules [31,32,38], and bending vibrations of  $\text{NH}_2$  groups [20,29]. These bands are overlapping, what does not allow the clear determination of their exact positions.

### Conclusions

The results of these studies indicate unambiguously that the mechanochemical interaction in mixtures of solid organic acids with silicate carriers ( $\text{SiO}_2$  or layered silicates) involves physico-chemical processes which take place on the freshly formed surfaces obtained in the course of MA. These processes are neutralization reactions between the components of the



**Figure 10.** IR spectra of the  $\text{SiO}_2$  + amino acetic acid mixtures before (1) and after the MA for 3 (2) and 5 minutes (3); m. r.  $\text{SiO}_2$ :acid = 8:1

mixture. They provide uniform thin-layer distribution of the organic phase over the surface of the carriers.

It has been proved by spectrochemical analyses that mechanochemical interactions of layered silicates with monocarboxylic organic acids involves quantitative neutralization of the protons of carboxyl groups and the basic centers of silicates on the freshly formed silicate surfaces, with the release of water molecules into the gas phase.

For dicarboxylic acids, unlike monocarboxylic acids, this process is carried out in two stages. At the first stage (which is more fast, within 1 minute), a proton of one of the two carboxyl groups of each acid molecule is substituted. Only after that the second COOH group enters the reaction, which is noticeably slower at this stage.

With silicon dioxide used as the carrier, in the cases of mono-, polycarboxylic, and aromatic acids, water molecules adsorbed on the  $\text{SiO}_2$  surface provide chemical links between carrier and monomeric acid molecules:  $\text{SiO}_2$  – adsorbed water – acid. Water molecules form rather strong hydrogen bonds with the basic surface centers of  $\text{SiO}_2$  and with the hydroxyl fragments of the monomeric acid molecules.

In the case of hydroxy acids, particularly aromatic ones, the mechanochemical interaction with  $\text{SiO}_2$  is involved both with basic and acidic surface centers of  $\text{SiO}_2$ . Hydroxyl (phenolic) groups interact with acidic centers, while hydroxyl fragments of carboxyl groups, similarly to the hydroxyl fragments of COOH groups of the acids, form hydrogen bonds with adsorbed water molecules that are bound through hydrogen bonds with basic centers on the  $\text{SiO}_2$  surface.

It is established that amino groups of amino acetic acid are partially deprotonated when interacting with basic active centers of the  $\text{SiO}_2$  surface, while  $\text{COO}^-$  groups interact with its acidic centers.

It is evident that the surface fixation of organic substances on the carriers, as a consequence of mechanochemical interaction, in any variation, alters the pharmacokinetics and allows avoiding ulcerogenic action. In cosmetic preparations this allows reducing the skin-irritating effects of organic acids.

### Conflicts of Interest

The authors declare no conflict of interest.

### Acknowledgments

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