Spectroscopic and X-ray structural investigations of the active calcium preparation

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Abstract. Structural studies of calcium citrate obtained by IR irradiation of calcium carbonate and citric acid in various ratios by spectroscopic and X-ray structural analysis has been carried out. It is shown that in the obtained samples of calcium carbonate there are polymorphic states in the form of aragonite, vaterite, calcite, as well as ikaite and in calcium citrate complex calcium compounds with different coordination numbers are observed.

1 Introduction

Basically, the cause of most diseases is the lack of trace elements in our body. Imbalance of trace elements can lead to a serious illness of such organs as the kidneys, heart, liver, lungs, intestines, spleen, etc.

One of these trace elements is calcium, which in the human body acts as a calming agent for the nervous system and is necessary for normal sleep. It is very important for the chemical balance of the body, normalizes the functioning of the nervous system, muscle functions, regulates the heart rhythm. It is necessary for normal blood clotting, activation of enzymes [1].

The problem of calcium deficiency, which leads to frequent fractures and injuries of the spine and other bone tissues, reduced growth, muscle contraction, muscle cramps, fragility, separation of the nail plate, poor growth, soreness of the gums, mouth and caries is one of the most pressing problems. The creation of easily digestible calcium preparations and the study of their structural characteristics is one of the important tasks today [2].

Even though blood calcium makes up only a small percentage of total body calcium, the body works very hard to keep blood calcium levels within a very narrow range of normal values. Bones are constantly remodeling (breaking down and rebuilding) to keep blood calcium levels within normal limits. The body automatically moves calcium out of the bones if a person does not get enough calcium from their diet or supplements. If the body continues to break down more bones than it replaces to maintain calcium levels in the blood, over time this situation can lead to osteoporosis, which literally means porous bones.

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Calcium supplements are available in many different forms such as tablets, capsules, gummies, gummies including chocolate, and various liquid forms. Calcium carbonate is the most popular form of calcium and is fine for most people, especially when taken with food [3].

However, people who do not produce enough stomach acid or are taking acid-blocking drugs are advised to take a more lightly ionized form, such as calcium citrate or calcium bound to malate, aspartate, or lactate. Calcium in these forms has some advantages over calcium carbonate because calcium is more easily released from the carrier molecule. The problem with this kind of calcium is that the carrier molecules expand in volume because they are larger than the carbonate. Thus, it takes four times as many tablets or capsules to provide the same level of elemental calcium compared to products containing calcium carbonate.

Currently, calcium salts such as glycerophosphate, gluconate, carbonate, lactate, citrate, chloride, phosphate, and many others are used in medical practice [2, 7]. The pharmacokinetics of the drug calcium citrate has its own characteristics. Calcium is absorbed from the intestine in a soluble ionized form. The dissolution of the drug occurs better in the acidic environment of the stomach. Dissolved ionized calcium penetrates well into all tissues and through the placental barrier enters breast milk. It is excreted from the body mainly with feces, about 20% - with urine.

An important feature of calcium citrate is that it does not stimulate the formation of kidney stones, which is important for long-term use. This is due to the fact that the citrate salt reduces the amount of oxalates in the urine.

The bioavailability of a drug is determined by the rate and degree with which the active substance is absorbed from the dosage form, becomes available at the site of the intended therapeutic effect.

At night, there is an accelerated release of mineral salts from the body (circadian acceleration of resorptive processes in the bone). Therefore, it is advisable to take calcium supplements after dinner and in the evening, which will prevent an accelerated loss of calcium in the second half of the night, especially with a reduced level (or absence) in the intestine. There is a negative dose-dependent effect of the pharmacotherapeutic activity of calcium: in low doses, this biometal is absorbed better than in high doses. In this regard, it is more rational to take the drug several times a day. For different age groups, there are different physiological norms for calcium intake.

In this work, activated calcium was obtained, which is in the form of a chelate compound, and its structural characteristics were studied by X-ray diffraction analysis.

We have developed a new type of calcium citrate suspensions using infrared radiation. The drug called "Activated calcium" is an aqueous homogeneous finely dispersed suspension. The starting products are calcium carbonate (SSt 4530-76) and citric acid (SSt 3652-69), which are mixed in an equivalent 1:1 (in gr.) ratio in an aqueous medium (distilled water SSt 6709) under IR irradiation in various ranges wavelengths and time. Radiators of the series: K, R, G, Z, allow you to receive radiation in the range from 8 to 50 microns.

To obtain the "Activated Calcium" suspension, calcium carbonate and citric acid dried in an IR oven for 30 minutes were dissolved in purified water. The dissolution of the ingredients was carried out in a stainless steel container with constant stirring and irradiation of the entire mass with special ceramic IR emitters. In this case, the temperature of the solution does not exceed 22^0C $\pm 2^0$C. To study the physico-mechanical, physico-chemical and pharmacological properties of activated calcium, different samples were prepared, which differed from each other in concentration, exposure time and ceramic lamps.

2 Methods

Activated calcium was obtained by mixing calcium carbonate (SSt 4530-76) and citric acid (SSt 908-2004) in an equivalent ratio in an aqueous medium, subjecting to IR irradiation at various doses.

X-ray diffraction analysis was carried out using a DRON-3M diffractometer. We used CuKα radiation separated by a nickel filter with a wavelength λ=1.542 Å. The operating voltage was 22 kV, and the anode current was 12 mA.

The principle of X-ray diffraction is based on the scattering of X-rays of the test subjects with subsequent fixation of the scattered rays by an ionization counter. The wavelength of X-ray radiation commonly used for studying polymers is 1.5418 Å (CuKα radiation). X-ray data quickly and quite unambiguously allow us to decide whether the sample under study is amorphous or crystalline, more precisely, amorphous-crystalline [16].

IR spectroscopic studies were carried out on a Specord 75 IR IR spectrophotometer in the wave number range of 4000...400 cm^{-1}, since absorption bands of almost all functional groups of organic molecules lie in this spectral range.

The basic principles and methods of IR spectroscopy are described in sufficient detail in the relevant literature [17]. Therefore, we will focus only on the most general principles of the method of preparing objects for research.

Methods for preparing samples are varied and depend on the nature of the object under study and the task of the study. In our work, we prepared samples by pressing a sample of calcium carbonate with KBr and applying a thick white liquid of calcium citrate to the surface and obtained thin films.

The method of pressing the test sample with an alkali metal halide is the most common method. The use of potassium bromide makes it possible to obtain a sample in the form of a transparent tablet. Pure, dry potassium bromide (150-200mg) - carefully ground with a solid sample (1.5mg) in an agate mortar with a pestle. The samples mixed with potassium bromide were placed in a mold, connected to a vacuum pump, evacuated for 2 min, and then pressed for 2 min without disconnecting from the vacuum system under pressure 7000kgf/cm^2 (7*10^8Pa).

Thermal analysis of the composites was carried out on a complex thermoanalytical installation "DERIVATOGRAF" system F.Paulik, J.Paulik, L.Erdei of the company "MOM" (Hungary) [5]. The measurements were carried out in the temperature range from room temperature to 8000C in an air atmosphere with a temperature rise rate of 8.5 deg/min.

3 Results and discussion

The structure of calcium carbonate and calcium citrate was studied by X-ray diffraction analysis, and the unit cell parameters were calculated from experimental data, which made it possible to evaluate the morphology of the obtained samples.

As can be seen from the experimental data, calcium carbonate has polymorphism in the form of calcite, aragonite, vaterite, and ikaite, which differ not only in lattice parameters but also in syngony, which characterize the activity of calcium carbonate to interact with other substances.

As we know, the interplanar spacing of the system is a function of the cell parameters. Knowing the value of the interplanar distance, it is possible to estimate the parameters of the cells by the optimization method, in which the interplanar distance is a function dependent on six parameters $d=f(a,b,c,\alpha,\beta,\gamma)$.

For the higher syngony, this dependence becomes simpler. We calculated the cell parameters and the size of the crystallites, which are associated with line broadening and were calculated using the Debye-Scherrer formula (tables №1, №2, №3, №.4).

The calculated values of the unit cell parameters by the optimization method for the obtained samples under various conditions have, *a=15.7 Å, b=7.8 Å , c=8.3 Å* and have rhombic, hexagonal and triclinic systems.

In the IR spectrum of citric acid in the disk with KBr at 1751 cm^{-1} and 1701 cm^{-1}, two intense and one weak at 1655 cm^{-1} bands of stretching vibrations of carbonyl groups are found. In the region of 3500-3200 cm^{-1} there is a group of absorption bands, which is associated with vibrations of variously associated hydroxyl groups of both alcohol and carboxyl fragments of the acid molecule. A characteristic feature is a broadened triplet with maxima at 3451, 3384, and 3296 cm^{-1}, which belongs to the stretching vibrations of the associated hydroxyl groups. The narrow intense peak at 3526 cm^{-1} corresponds in character to the stretching vibrations of the free hydroxyl group.

Absorption bands in the region of 1217-1431 cm^{-1} correspond to bending vibrations of hydroxyl groups, and in the region of 1130-1180 cm^{-1} intense absorption bands are found corresponding to stretching vibrations of *C-O* bonds.

In the IR spectrum of calcium citrate in the range of stretching vibrations of *C=O* groups, one intense wide band is found at 1595 cm^{-1}, corresponding to asymmetric stretching vibrations of the same type of anions of carboxyl groups, a group of absorption bands of stretching vibrations of *OH*-groups is transformed into one wide intense band with a maximum at 3428 cm^{1}, which, based on the structure of citric acid, can be attributed to the stretching vibrations of the tertiary hydroxyl group involved in the formation of intra- and intermolecular associates.

Table 1. The cell parameters and the size of Calcite, calculated using the Debye-Scherrer formula

Parameters	Calcite				
	Crystalline reflexes				
Maximum position 2θ, (deg.)	23.25	29.78	36.5	40.35	47.0
Interplanar spacing d, (Å)	3.826	3.0	2.462	2.235	1.933
Peak width at 0.5 height β, (deg.)	0.25	0.15	0.35	0.15	035
Crystallite size l, (Å)	360.755	609.387	265.764	627.42	276.014

Table 2. The cell parameters and the size of Aragonite, calculated using the Debye-Scherrer formula

Parameters	Aragonite				
	Crystalline reflexes				
Maximum position 2θ, (deg.)	47.75	37.0	31.2	42.0	50.0
Interplanar spacing d, (Å)	1.905	2.714	2.867	2.273	1.814
Peak width at 0.5 height β, (deg)	0.35	0.25	0.25	0.15	0.1
Crystallite size l, (Å)	276.014	368.531	366.869	626.027	946.235

Table 3. The cell parameters and the size of Vaterite, calculated using the Debye-Scherrer formula

Parameters	Vaterite			
	Crystalline reflexes			
Maximum position 2θ, (deg.)	48.8	42.5	32.75	40.25
Interplanar spacing d, (Å)	1.866	2.12	2.73	2.23
Peak width at 0.5 height β, (deg)	0.1	0.25	0.44	0.15
Crystallite size l, (Å)	970.025	380.438	18.38	627.42

Table 4. The cell parameters and the size of Calcium citrate, calculated using the Debye-Scherrer formula

Parameters	Calcium citrate					
	Crystalline reflexes					
Maximum position 2θ, (deg.)	11.93	21.2	23.27	25.75	29.5	31.5
Interplanar spacing d, (Å)	7.418	4.191	3.754	3.46	3.028	2.84
Peak width at 0.5 height β, (deg)	0.1	0.1	0.1	0.1	0.1	0.15
Crystallite size l, (Å)	888.19	898.72	902.62	906.16	913.49	611.8

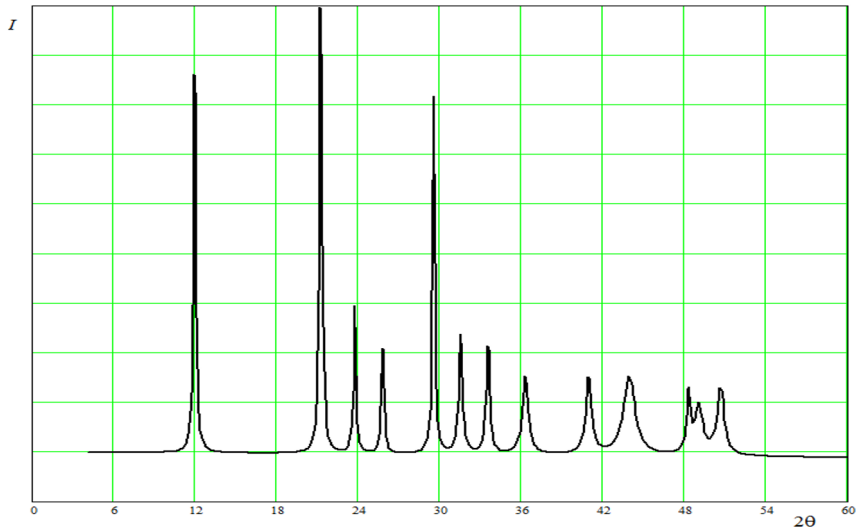

Fig. 1. Diffractogram of calcium citrate

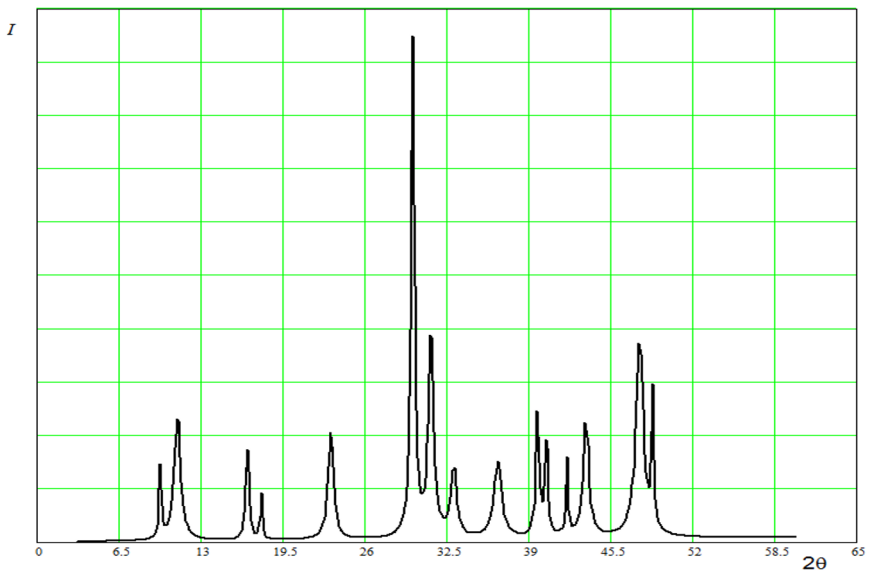

Fig. 2. Diffractogram of active calcium

As can be seen from the experimental data, the ratio of different phases in calcium carbonate is one of the important qualities in the production of calcium citrate, which show high absorption of calcium by the body.

X-ray diffraction analysis showed that an increase in the ratio of aragonite in the feedstock leads to the formation of calcium citrate - a coordination compound characterized by a lower content of calcium carbonate in the composition, which are connected by the aragonite syngony.

4 Conclusions

Thus, it can be said that when obtaining calcium citrate with good digestibility by the body, the main parameter is the polymorphism of calcium carbonate, in which the ratio of the calcite, aragonite and vaterite phases plays an important role in the production of calcium citrate.

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