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THERMAL ANALYSIS OF SOME PHARMACEUTICALLY RELEVANT SYSTEMS OBTAINED BY SOL-GEL TECHNIQUE

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Abstract

Thermal analysis has been performed of xerogels obtained by encapsulation of sodium thiosulfate (systems I and II), glycerol with I_2/KI (system III) and urea with I_2/KI (system IV) in silica gel. DTA, TG and DTG of the xerogels with thiosulfate differed markedly depending on the thiosulfate content. At the 22% thiosulfate content in the original silicic acid solution used for the preparation of the xerogel, a single exothermic peak appears in the DTA trace assignable to the combustion of elemental sulfur derived either from the reaction between silicic acid and the thiosulfate or from the thermal degradation of the latter. When the thiosulfate content in the original solution is raised up to 60%, the peak is split into two symmetrical components, one (at 553 K) attributable to combustion of the more finely dispersed sulfur and the other (at 703 K) to sulfur particles of coarser morphology. The former is likely to be formed by chemical interaction of the components of original solution and the latter is due to thermal degradation of residual thiosulfate.

The main features of a DTA, TG and DTG obtained from xerogel III are exothermic events recorded in the DTA trace suggesting that after the loss of iodine, thermal degradation of glycerol takes place with the onset at 523 K leaving a combustible solid. Under these conditions, glycerol alone distilled out with no evidence for degradation.

A derivatogram of xerogel **IV** is characterized by initial sublimation/evaporation of urea and iodine followed by partial condensation of urea to afford biuret and eventually cyanuric acid.

Keywords: DTA, DTG, glycerol, iodine, orthosilicic acid, potassium iodide, silica gel, sodium thiosulfate, sulfur, TG, urea

Introduction

The method of embedding various molecules, both organic and inorganic, in inorganic oxides through sol-gel processes is an area of intense interest worldwide. The sol-gel process consists in producing inorganic matrices through gelation of colloidal

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suspensions (sols). When the process is conducted in the presence of a guest molecule, it becomes encapsulated in the gel network being formed to produce a system of specific properties. Generally, the entrapped molecules retain much of their characteristic physical and chemical properties and are accessible to external reagents through the pore network [1].

One of the common precursors used for preparation of such systems is orthosilicic acid. It can be obtained either from soluble inorganic silicates, for instance sodium silicate [2] or by hydrolysis of tetraalkyl silicates, in particular tetraethyl or tetramethyl silicate [3].

Orthosilicic acid is unstable in solution and gradually undergoes condensation reactions leading to oligo- and polysilicic acids forming colloidal suspensions and eventually gels [4–7]. These, after drying, afford solid amorphous materials called xerogels.

From the pharmaceutical point of view, silica gels can be utilized as non-toxic and biocompatible carriers of various substances, including drugs [8–10] in controlled drug delivery.

An outstanding position of silica gels among sol-gel products lies in that an extraordinarily wide range of microstructures may be formed ranging from dense particles in colloidal suspensions to fractal structures with widely disparate degrees of branching [11].

The purpose of this contribution was to prepare and investigate thermal decomposition of silica xerogels with embedded pharmaceutically relevant guest molecules, sodium thiosulfate used in dermatology and the components of Lugol's solution (I_2/KI) used in laryngology. As a matter of fact, the preparations are usually stored at ambient temperature, but from the chemical point of view it was interesting to investigate their behaviour upon heat treatment. In this respect of particular interest was the xerogel with embedded chemically and thermally labile thiosulfate.

Experimental

Preparation of orthosilicic acid

Dilute solutions of orthosilicic acid were obtained from water glass (Na_2SiO_3 solution) by a procedure reported by Yoshida [12]. Thus, a water glass R-145, manufactured by Chemical Works 'Rudniki', Poland (sp. gravity 1.45 g cm^{-3}; SiO_2/Na_2O molar ratio of 2.5) was diluted (1:5) with distilled water and fed onto a glass column (500 x 40 mm i.d.) loaded with a cation-exchange resin (Amberlite IR 120 in the H^+ form). The concentration of orthosilicic acid in the eluate was approx. 1 per cent based on SiO_2.

Preparation of the silica-based systems

One hundred millilitres of the silicic acid solution was blended with 50 mL of:

22% thiosulfate pentahydrate solution (formulation **I**);
60% thiosulfate pentahydrate solution (formulation **II**);

20% I_2/KI solution in glycerol (formulation **III**)

20% aqueous solution of urea and I_2/KI taken in equimolar proportion (formulation **IV**).

The gelation times of **I**, **III** and **IV** were 48 h each, and that of **II** was 55 min.

The gels were dried at 323 K, pulverized and kept in closed vessels.

Formulations **I** and **II** contained elemental sulfur formed on account of interaction between orthosilicic acid and thiosulfate:

$$S_2O_3^{2-}+2H^+=S+SO_2+H_2O$$

A procedure for the preparation of **I** and **II** has been patented [13] and a preliminary study of the system hydrated silica – sodium thiosulfate – sulfur has been reported [14]. Xerogels **I** and **II** contained 50.6 and 63.67% of $Na_2S_2O_3$, respectively.

Determination of the iodine content in xerogels containing I_2/KI

The iodine content in the xerogels was determined by titration of an approx. 1 g finely powdered sample with a standardized sodium thiosulfate solution using starch as indicator. Xerogel **III** contained 1.94% of iodine, 1.26% of KI, 70% of glycerol and 26.8% of silica gel, whereas xerogel **IV** contained 0.9% of iodine, 0.6% of KI, 45.5% of urea and 53% of silica gel.

Thermal analysis

Thermal decomposition of the xerogels was carried out on a Model OD-103 derivatograph (MOM, Hungary) under identical conditions. A 200 -mg sample was placed in a platinum crucible of 9.5 mm in diameter and heated at a rate of 5 K min^{-1} up to approx. 1173 K. The DTA, TG and DTG traces were recorded in air atmosphere. α-Al_2O_3 was used as a reference material.

Results and discussion

Silica xerogel

In the DTA, TG and DTG curves of the silica xerogel presented previously [14], the loss in mass begins at 313 and is completed at 453 K (TG). It is accompanied by a massive endothermic effect (DTA) due to evaporation of physically adsorbed water followed by subsequent condensation of silanol groups of the gel:

$$\equiv Si–OH+HO–Si\equiv=\equiv Si–O–Si\equiv+H_2O$$

Another endothermic effect emerging in the DTA curve at approx. 473 K is due to condensation of the more firmly bound silanol groups, as indicated by a further loss in mass in the TG trace. These findings are compatible with the literature reports on thermoanalytical characterization of silicic acid gels [15, 16].

*Xerogels **I** and **II***

There are some interesting features in the DTA, TG and DTG curves of the xerogels **I** and **II** obtained from the silicic acid solutions and sodium thiosulfate (Figs 1a and 1b). As it has been reported previously [14], sodium thiosulfate is partially decomposed by silicic acids to afford finely dispersed elemental sulfur. Again, sulfur alone, embedded in silica gel, burns at a temperature around 573 K as shown in Fig. 1c. On the other hand, sodium thiosulfate pentahydrate loses water molecules around 400 K [14] and the anhydrous salt is decomposed over the range 583 – 658 K as reported by Picon [17] to release elemental sulfur.

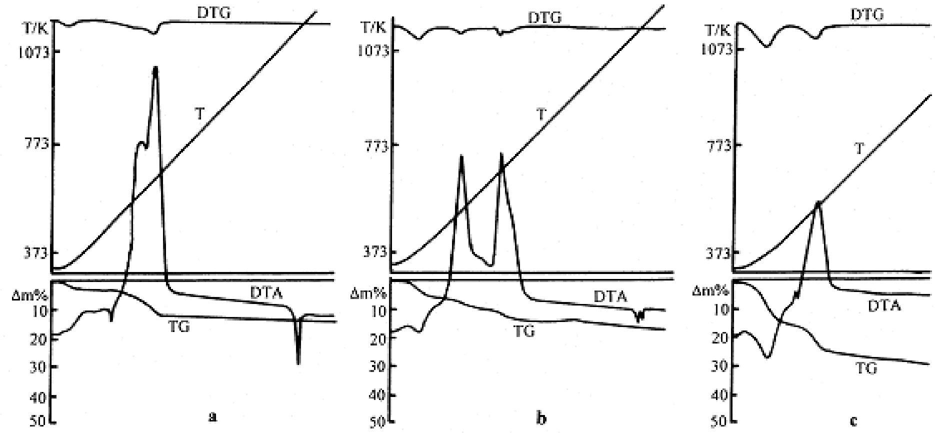

Fig. 1 DTA, DTG and TG curves of thermal decomposition of xerogels **I** and **II** obtained respectively from: a – a 22% sodium thiosulfate pentahydrate solution in 1% orthosilicic acid; b – a 60% sodium thiosulfate pentahydrate solution in 1% orthosilicic acid; c – of elemental sulfur embedded in silica gel

A similar pattern is followed in the DTA, TG and DTG curves of xerogel **I** obtained from the 22% thiosulfate solution (Fig. 1a), but the DTA peak is displaced to a higher temperature (623 K).

When the quantity of sodium thiosulfate in the xerogel is considerably increased (xerogel **II**), the DTA peak is split into two almost symmetric components (Fig. 1b), one centred around 553 K and the other around 703 K. This splitting can be interpreted as being due to the presence of two distinct morphological forms of elemental sulfur, one more finely dispersed and the other of coarser morphology. One of these forms is likely to be derived from chemical degradation of the thiosulfate by silicic acids occurring at the preparation step of the formulation, and the other is produced by thermal degradation of the thiosulfate taking place over the range 583–658 K [17].

An endothermic peak around 1170 K can be assigned to the melting of sodium sulfate formed by partial oxidation of the sulfite left after degradation of the thiosulfate:

$$Na_2S_2O_3=Na_2SO_3+S$$

*Xerogel **III***

The DTA, TG and DTG of xerogel **III** (Fig. 2a) is characterized by the dehydration step peaked at ca 373 K followed by two distinct steps in the mass loss, one with the onset at 413 K and the other at 553 K. The former, endothermic, can be attributed to volatilisation of glycerol (b.p. 563 K) and iodine, and the other, with a series of exothermic events and a steady loss in mass, to combustion of a residue left after partial degradation of glycerol. The small endothernic peak around 933 K is due to the melting of KI (lit. m.p. 933 K)

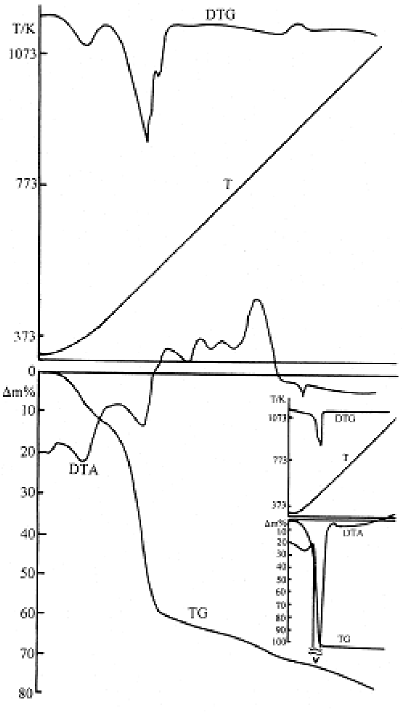

Fig. 2 DTA, DTG and TG curves of xerogel **III** obtained from a 20% I_2/KI solution in glycerol in a – 1% orthosilicic acid and b – of glycerol

A separate run with pure glycerol (Fig. 2b) has shown that glycerol distills out without decomposition. It can thus be concluded that in the presence of silica glycerol

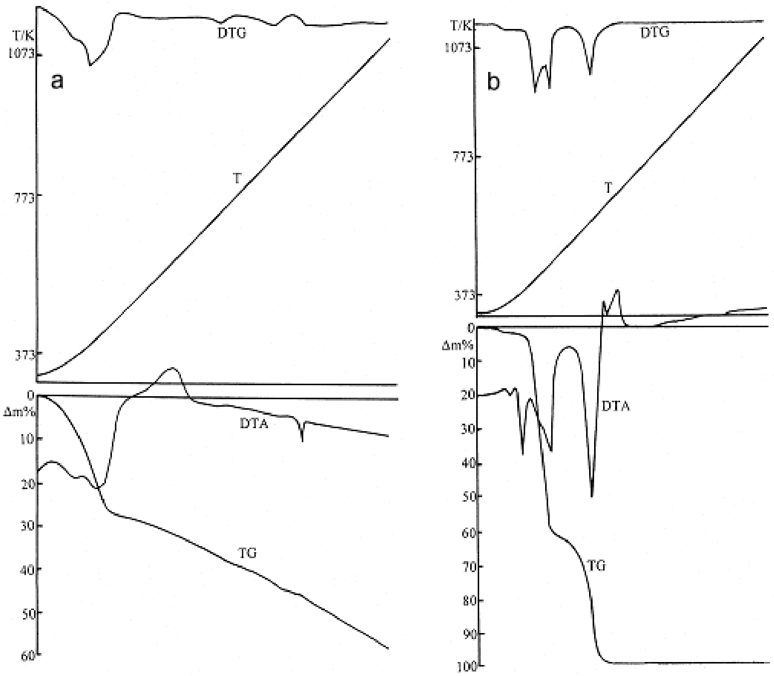

Fig. 3 DTA, DTG and TG curves of xerogel **IV** obtained from a 20% solution of urea and I_2/KI taken in equimolar quantities in 1% silicic acid (a) and of urea (b)

is firmly bound on account of hydrogen bonds between silanol groups of the gel and hydroxyl groups of glycerol and undergoes thermal degradation with the onset at ca 553 K. As far as the TG and DTG curves of xerogel III are concerned, it is difficult to draw a clear distinction between the end of the loss of water and the onset of the loss of glycerol. As seen in Fig. 2b, glycerol alone distills off undecomposed, while when embedded in the gel it undergoes thermal degradation (Fig. 2a). The 12% mass loss in the TG curve up to ca 413 K can be assigned to the loss of water and partial evaporation of glycerol. Subsequent 48% loss in weight can be attributed to further evaporation of glycerol followed by its degradation and combustion (exo effects) accompanied by a ten or so per cent mass loss extending up to ca 1070 K. The residue (24%) is composed of silica and KI.

*Xerogel **IV***

In the DTA, TG and DTG curves of this xerogel (Fig. 3a) there is a rapid loss of water molecules up to ca 375 K and a further gradual loss in mass due to sublimation/evaporation of urea and iodine (urea m.p. 406–408 K). However, no distinction can be made between the loss of either. Urea has been known to undergo condensation reaction over the temperature range 423–443 K [18] to afford biuret, $H_2NCONHCONH_2$. This in turn, decomposes at the m.p. (465.5–466 K) [19] to give cyanuric acid (1,3,5-triazine-2,4,6-triol). These data are roughly consistent with three endothermic peaks in the DTA, DTG and TG curves of urea (Fig. 3b) at 373, 473 and 633 K corresponding, respectively, to the degradation of urea, biuret and cyanuric acid. All the three events are accompanied by massive losses of volatile products among which ammonia was qualitatively detected as the main constituent. Theoretical loss in mass due to condensation of two molecules of urea is 13.6%. That in Fig. 3b is as high as 60% thus indicating partial sublimation of urea. The exothermic peak at 613 K (Fig. 3a) can be assigned to the combustion of a solid residue left after degradation of cyanuric acid, while that at 903 K is due to the melting of KI.

In the DTA, TG and DTG curves of xerogel IV (Fig. 3a), particular endothermic peaks seen in Fig. 3b are absent, probably due to interactions of urea, biuret and cyanuric acid with residual hydroxyl groups of the gel. Thus, it can only be hypothesized that up to 393 K water is released (11%), followed by the loss of ammonia, urea and iodine up to 493 K (16%) and thermal degradation of biuret (ca 27% loss in mass; exo effect at 613 K) along with ongoing dehydroxylation of silica gel [15, 16].

Conclusions

The thermal analysis techniques used in this work turned out to be particularly useful for identifying different morphological forms of elemental sulfur derived from chemical and thermal degradation of sodium thiosulfate embedded in silica gel. They proved also helpful in following thermal degradation steps of other pharmaceutically relevant guest molecules such as the components of Lugol's solution and glycerol.

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