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THE STABILITY OF DRUG ADSORBATES ON SILICA

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ABSTRACT

Colloidal and porous silicas are used as carriers in solid, semisolid and liquid dosage forms. Adsorption of active ingredients onto their large surface areas can be used to regulate drug release or for the uniform distribution of drug in single dose units with a very low drug content. In the adsorbates the contact between drug and carrier surface on the molecular level can be of great importance for the chemical stability of drug preparations. This is demonstrated by the following examples:

Hydrolytic degradation of acetyl salicylic acid in dry silica adsorbates is mainly determined by alkaline impurities of the carrier and strongly adsorbed water on the silica surface. The "catalytic" action of silicas is, therefore, directly dependent on the preparation technique of the carrier. Propantheline a cationic ester

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compound is adsorbed on silica from aqueous solution. In aqueous silica suspensions and in dry adsorbates the ester hydrolysis is controlled by the pH, the neutral salt content, and buffer substances, due to different adsorption mechanisms.

The oxidative degradation of butylhydroxyanisole in silica adsorbates was also found to be enhanced in the presence of alkaline impurities. The oxidation of linoleic acid methylester in oleogels of colloidal silica proved to be influenced both by carrier impurities and the specific adsorption of intermediates (peroxides) onto the surface.

INTRODUCTION

The concept of drug deposition on insoluble hydrophilic inorganic carriers is of great interest both in terms of the controlled enhancement of drug dissolution rate and/or an uniform distribution of low dosed drugs in single-dose application forms (1,2). Silica is of outstanding importance as a carrier material for this technique due to its excellent physicochemical and physiological properties and the large specific surfaces of colloidal and porous silica preparations, available for drug deposition (3).

In surface deposits of drugs of the adsorbate type the single drug molecules are uniformly distributed over the surface of the carrier and bound by specific adsorption sites. The stability of the drug may, however, be influenced by the catalytic action of the active surface sites of the carrier, impurities of the excipient or adsorbed water at the solid surface. At surface coverages

$\theta \leq 1$ each drug molecule in the deposit is in contact with the carrier and simultaneously exposed to the atmosphere, allowing oxygen or water molecules to attack reactive sites directly from the gas phase.

The main interest of this article is to demonstrate specific features of some degradation processes on silica surfaces. Representative drug models were chosen which were sensitive to hydrolytic or oxydative actions. These were used to evaluate the influence of different particle and surface structures of the silica carriers, their typical impurities as well as the humidity of the storage climate.

MATERIALS

The silica carriers used in our experiments were all of the hydrophilic amorphous type, characterized by reactive silanol groups on the surface and a nonreactive SiO_2 frame work (4) (Tab. 1). The flame hydrolyzed products Aerosil 200 (A 200) and HDK N 20 are composed of nonporous colloidal particles with traces of adsorbed HCl form the combustion of $SiCl_4$ (3). Silicas produced by sol-gel transformation of Na-silicates - Syloid 244, KG 60 - are porous as well as being particulate and are obtained by hydrolytic polycondensation of polyethoxysiloxanes (5). They contain impurities such as Na_2O, Fe_2O_3, Al_2O_3, or NH_3.

As examples of hydrolyzable drugs the esters acetylsalicylic acid (ASA) and propantheline bromide (Prop), a cationic aggrega-

TABLE 1: SILICA EXCIPIENTS

Product	Particle size	Pore size (nm)	Spec. surface $m^2\ g^{-1}$	Method of manufact.	Impurities [%]				
					Na_2O	Fe_2O_3	Al_2O_3	HCl	NH_3
Aerosil 200 1) [A 200]	10-40 nm	non porous	220	Flame hydrolysis of $SiCl_4$	--	< 0,003	< 0,05	< 0,004	--
HDK N 20 2)	5-30 nm	non porous	207	Flame hydrolysis of $SiCl_4$	--	< 0,005	< 0,05	< 0,004	--
TK 900 1)	2-15 µm	non porous	160	Electric arc	0,007	0,093	0,100	/	--
Syloid 244 3)	~ 2 µm	18	480	Sol-Gel	0,136	0,012	0,185	/	--
Kr 36 4)	~ 1 mm	14	510	Hydrolytic polycondensation of polyethoxysiloxane	0,002	0,004	--	/	0,132
KG 60 5)	~ 0,5 mm	6	550	Sol-Gel	0,100	0,016	0,093	/	--

1) DEGUSSA, Frankfurt a.M., FRG 2) Wacker Chemie, München, FRG 3) Grace, Worms, FRG
4) own development (5), 5) E. Merck, Darmstadt, FRG

ting drug, were selected. While ASA shows no adsorption from aqueous solution onto silica surfaces (6) Prop is strongly adsorbed from aqueous media (7). Butylhydroxyanisole (BHA) was the drug model used to study the oxydative degradation of phenolic compounds in silica adsorbates. Autoxidation was monitored in silica suspensions of linoleic acid methylester (LME) (Tab. 2).

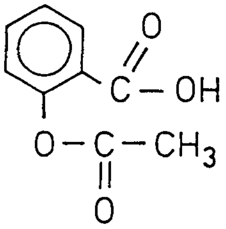
PREPARATION OF THE ADSORBATES

Numerous articles deal with the chemical stability of drugs, in which the drugs are deposited on the silica surface as crystals or thick amorphous layers (1,8,9). The surface deposites used in our experiments, however, were prepared in a different manner by establishing adsorption equilibria at the silica/solution interface by means of an appropriate solvent. By this technique well defined drug adsorbates on the silica carriers were obtained. In these adsorbates the position of the drug molecules on the carrier surface can be evaluated from adsorption data - surface coverage, heat of adsorption - and by IR and UV spectroscopy of the adsorbed molecules (4).

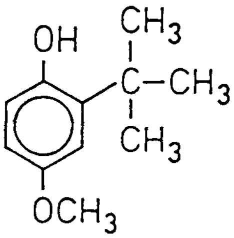
Acetylsalicylic acid (ASA)

ASA was adsorbed from dichlormethane solution on silicas by a standard procedure: After equilibration of the silica with the drug solution at 20^{0}C (within 12 h), the adsorbates were removed from the liquid phase by filtering or centrifugation and then dried in a vacuum. The dry adsorbates were stored over P_2O_5 and the initial

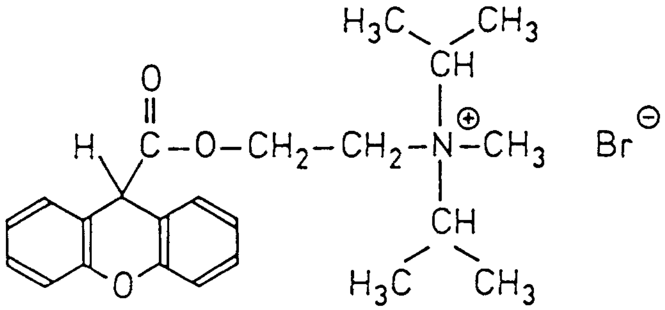
TAB.2. — DRUG MODELS



Acetylsalicylic acid
ASA



Butylhydroxyanisol
BHA



Propantheline bromide
Prop

Linoleic acid methylester
LME

contents of ASA and salicylic acid determined before starting the stability experiments.

In Fig 1 the position of an ASA molecule in adsorbates on silica surfaces is given schematically. The drug is adsorbed by hydrogen bonds between surface silanol groups and proton acceptor groups of ASA, the ester linkage or the π electron system of the ring. This adsorbate's structure was deduced from heats of adsorption - 17 kJ mol^{-1}, and IR spectra of the adsorbates (6). In addition, strongly adsorbed water molecules are present in the drug adsorbates on the silica carriers.

Butylhydroxyanisole (BHA)

For the adsorption of BHA onto the silicas the same procedure was used, except that cyclohexane as solvent was employed. For the structure of the adsorbates it is supposed that the BHA molecules are flatly attached to the surface, fixed in this position by hydrogen bonds between the phenolic groups and the silanol groups of the silica (Fig. 2) (10).

Propantheline bromide (Prop)

In contrast to ASA and BHA the aggregating cationic Prop was adsorbed from aqueous solution onto the silica surface (Fig 3) (11). Depending on the equilibrium concentration the Prop cations are primarily bound to the silica surface by ion exchange in the low concentration range (Fig. 3 A) according to

$$\mathrm{Prop}^{+} + \equiv \mathrm{Si} - \mathrm{OH} \rightleftharpoons \equiv \mathrm{Si} - \mathrm{O\ Prop} + \mathrm{H}^{+}$$

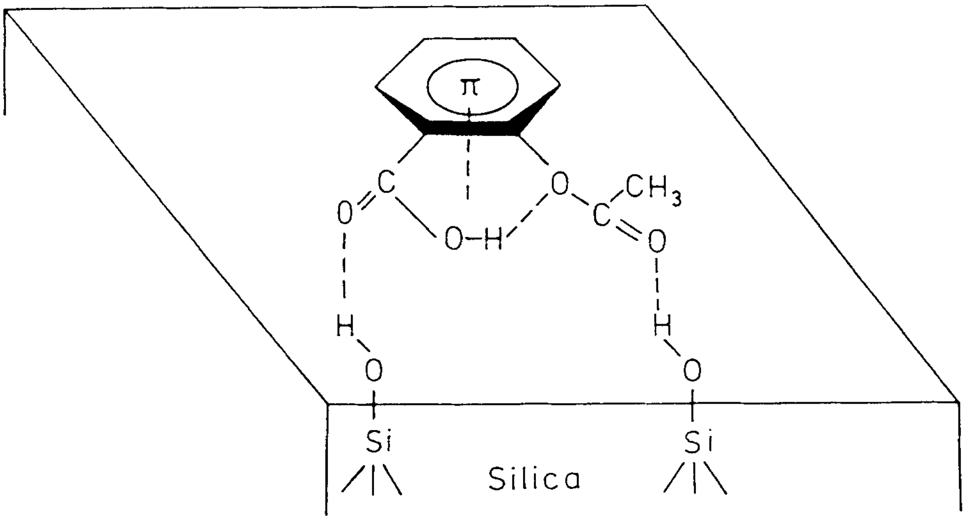


FIGURE 1

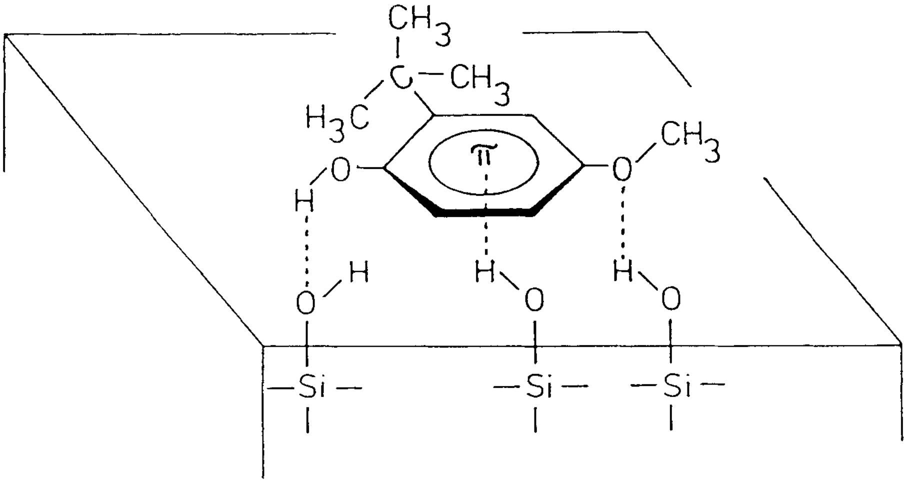
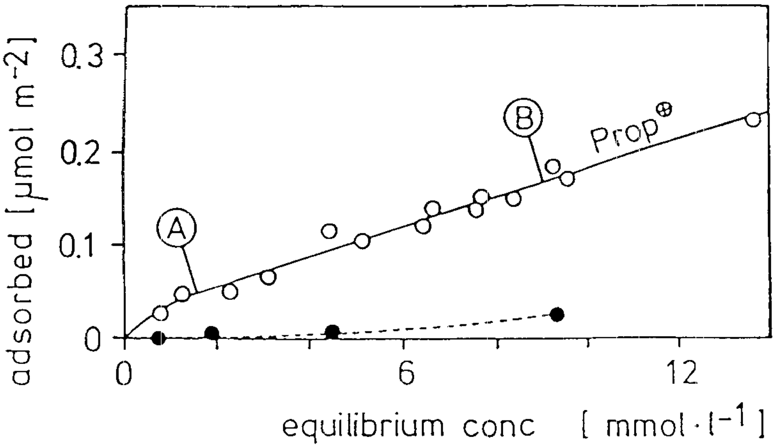
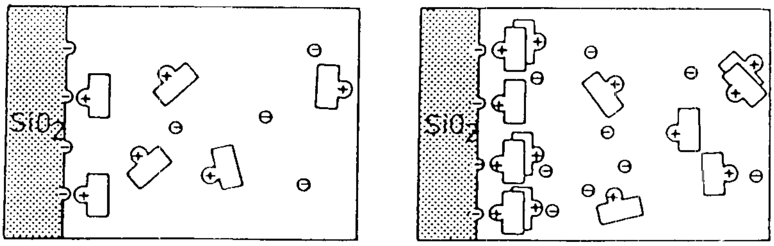


FIGURE 2



adsorption isotherm



adsorbate Ⓐ adsorbate Ⓑ

FIGURE 3

Structures of propantheline adsorbates on the silica surface, depending on the adsorption equilibrium.

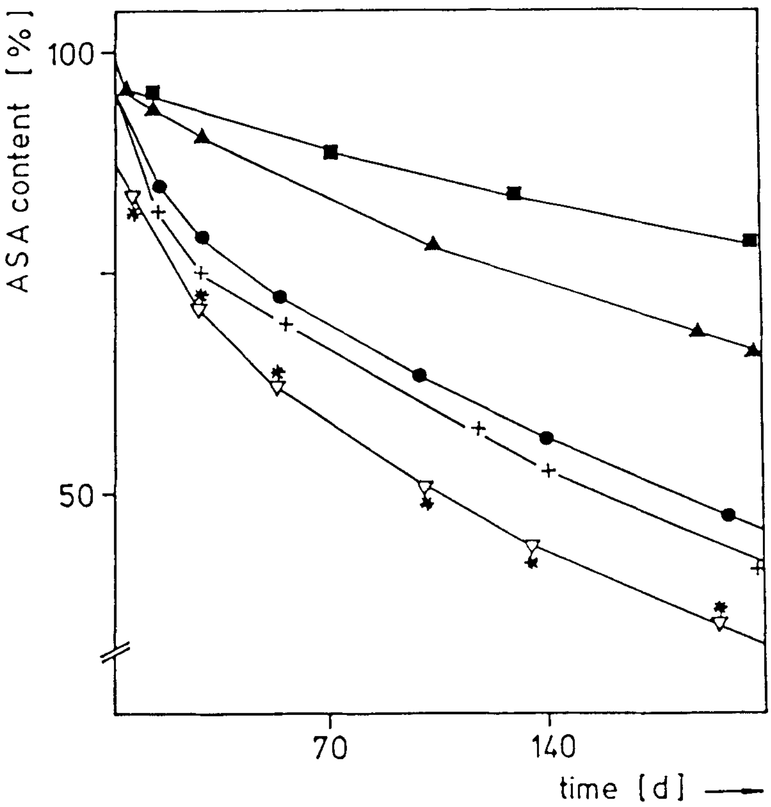


FIGURE 4

Hydrolysis of ASA in adsorbates on different silicas
(21°C ± 0,5; 32% R.H.; Θ = 1)

■ —— ■	HDK N 20	+ —— +	Syloid 244
▲ —— ▲	A 200	▽ —— ▽	KG 60
● —— ●	Kr 36	✱ —— ✱	TK 900

This mechanism is indicated by a decrease of the pH in the supernatant aqueous phase during the establishment of the adsorption equilibrium (i.e. pH 4,5 ⟶ pH 3,8) and by the difference in counter ion - $Br^{\ominus}$ - binding.

At higher concentrations Prop cations are adsorbed by hydrophobic bonding to the primary bound species which are themselves orientated perpendicular to the surface (Fig. 3 B). These Prop cations are accompanied to a great extend by their counterions, $Br^{\ominus}$, according to the concept of hemimicelle binding of surfactants (12).

The adsorption of Prop at the silica surface can be improved by increasing the pH and thereby increasing the cation exchange or by the addition of neutral salts with water structure-breaking counterions of Prop, such as nitrate (7). This effect can be attributed to an enhancement of ion pair adsorption, as controlled by hydrophobic and electrostatic interactions. Consequently the Prop ions are orientated with their polar head groups to the silica surface in the ion exchange layer. The secondarily attached Prop are orientated with their quaternary ammonium groups to the aqueous phase, with some of the counterions in close contact (in the Stern-layer) and some of them in the diffuse part of the electrical double layer at the interface.

HYDROLYSIS OF ESTER COMPOUNDS

Acetylsalicylic acid adsorbates

The loss of ASA in adsorbates on different silica carriers stored at 21°C and 31% rel. humidity (R.H.)1*) is shown in Fig. 4, de-

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1*) The adsorbates were stored in glas vessels with a controlled exchange of the gas phase to remove reaction products: "open storage conditions" (13).

monstrating a significant order of rank: The lowest rate of hydrolysis is observed on HDK N 20, followed by A 200 with a moderate stability for ASA, both being flame-hydrolyzed nonporous colloidal silicas. In contrast, the colloidal nonporous TK 900 as well as the porous KG 60 H show the strongest catalytic action on ASA degradation. The porous silicas Kr 36 and Syloid 244 are characterized by intermediate degradation rates of ASA.

This order of catalytic action of the silica carriers on ASA hydrolysis is obviously more dependent on the corresponding sum of catalytic impurities on their surfaces (i.e. Na_2O, Al_2O_3, NH_3) than on their structure characteristics (particle size, porosity, silanol group density). According to Edwards (14) the ASA degradation rate constant k is related to the $OH^\ominus$ concentration in an aqueous environment by

$$k = k' \; [OH^\ominus]$$

In the silica-ASA adsorbates an adsorption equilibrium also exists between water in the gas phase and on the silica surface. The adsorbed H_2O can react with alkaline impurities deposited on the silica surface present as $NaHCO_3$ and/or Na_2CO_3. Hydrolysis of these compounds releases OH-ions which then attack the ester linkages of adsorbed ASA molecules. Adsorbed NH_3 serves in the same way as an $OH^\ominus$ ion source.

On the other hand, surface bound HCl and Al_2O_3 (the latter being a Brönsted centre when adsorbed on SiO_2) can produce H_3O^+ ions with the adsorbed water, thus stimulating an acidic catalyzed ester hydrolysis (15).

These conclusions are supported by the direct correlation between the ASA hydrolysis-rates and the relative humidities of the storage climate which determine the water-"supply" in the adsorbates. From Fig. 5 it is clearly seen that ASA degradation is continuously accelerated by increasing the R.H. of the storage climate, when using the nonporous HDK N 20 as a support. The rate of ASA-degradation shows a maximum value at 86% R.H., however, if the porous Kr 36 is used as carrier for the ASA adsorbates (Fig. 6). This can be explained by capillary condensation at higher R.H. values (i.e. 98%), thereby filling the silica pores with aqueous phase. In the presence of a liquid water phase a quite different situation exists Dissolution of silica, dilution effects as well as the influence of water structure phenomena must now be considered as influencing ASA decomposition (16).

The mechanism of ASA hydrolysis in adsorbates on silica surfaces can now be discussed in detail, considering the amount of water molecules on the surface, available for ester hydrolysis. At 0% R.H. the porous Kr 36 adsorbate contains 7,3% H_2O, which corresponds to one H_2O molecule on each surface silanol group. Therefore the ratio between adsorbed ASA and water molecules is 1:10. To establish a close packed water monolayer on the silica surface, R.H. values > 60% are necessary, however. Even in a water vapor saturated atmosphere the amount of adsorbed water on the ASA adsorbates is far distant from forming "solution layers". On HDK N 20 the ratio is 1: 400 and on Kr 36, 1:150. For comparison, the ratio between ASA

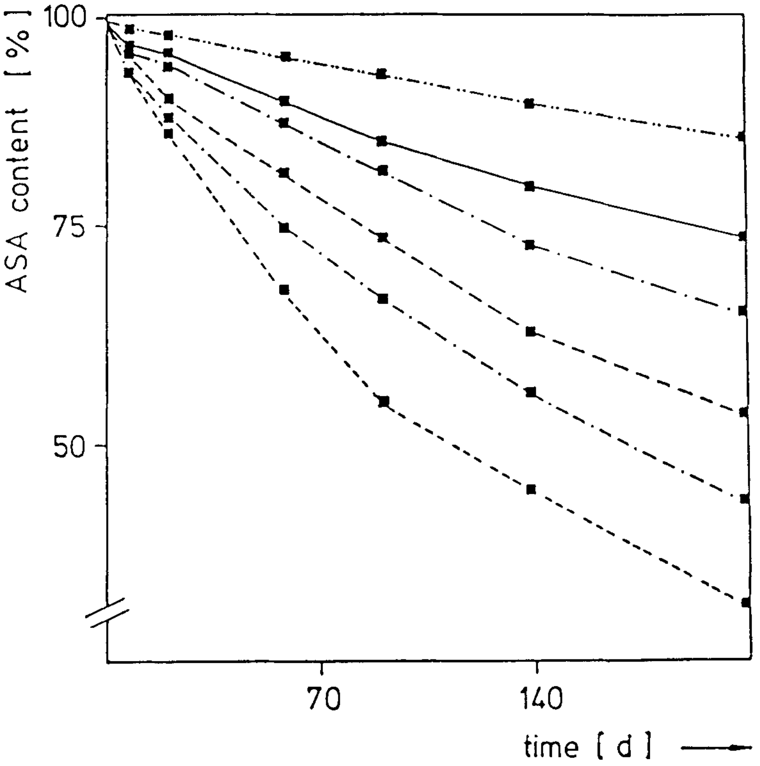


FIGURE 5

Hydrolysis of ASA in adsorbates on HDK N 20 at different relative humidities (21°C ± 0,5; $\theta = 1$)

■-··-··-■ 0% R.H.
■———■ 32% R.H.
■ · — · ■ 56% R.H.
■— —■ 77% R.H.
■-- · --■ 86% R.H.
■-----■ 98% R.H.

and water molecules in a saturated aqueous solution is 1:2500 at 21°C (17).

Therefore it is concluded that the diffusion rate of water molecules on the silica surface and/or $OH^{\ominus}$ and H_3O^+ ions, are the rate determining factors for ASA hydrolysis. It is here assumed that

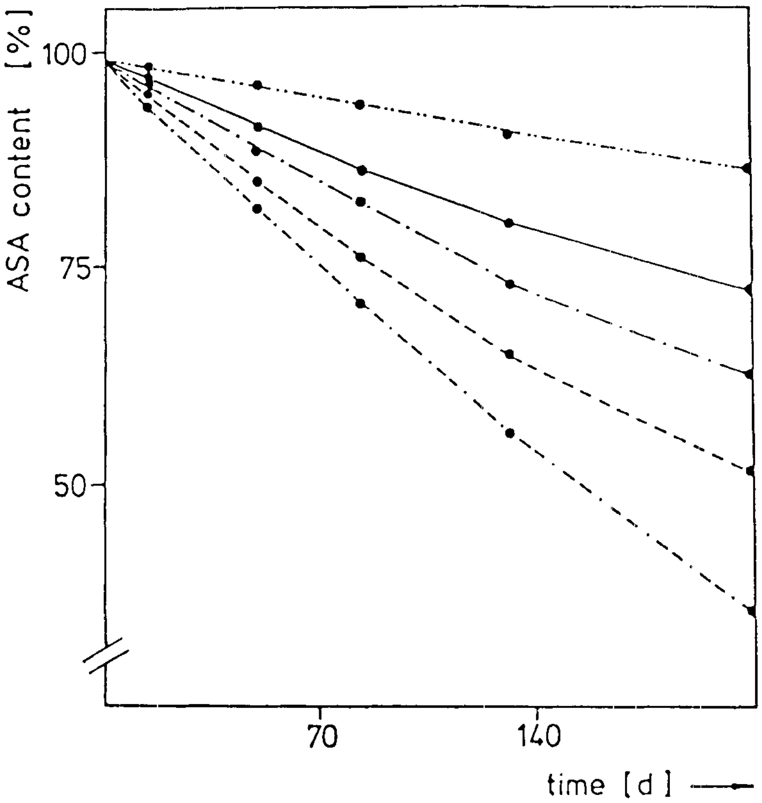


FIGURE 6

Hydrolysis of ASA in adsorbates on Kr 36 at different humidities ($21^{\circ}C \pm 0,5$; $\theta = 1$)

● —··—● 0% R.H.
● —— ● 32% R.H.
● ·—·—· ● 56% R.H.
● ---- ● 77% and 98% R.H.
●·—·—● 86% R.H.

at room temperatures only water molecules are able to migrate on the surface, while ASA molecules essentially remain on their adsorption sites. This view of ASA hydrolysis is confirmed by the strong correlation observed between the rate constant of ASA degradation and the water content of the adsorbates, based on a second order kinetics (17).

Propantheline-adsorbates

Considering the stability of propantheline (Prop) on silica surfaces there is a different stress on the drug during the production of the adsorbates, compared with ASA. In contrast to the adsorption of ASA from dichlormethane solution where water can be sufficiently excluded, the adsorbates of Prop are formed from aqueous solutions. Therefore hydrolytic degradation and adsorption become parallel processes in these systems.

In Fig. 7 the different loss of Prop decomposed to a quaternary ammonium alcohol and xanthene carboxylic acid is shown during the preparation phase of adsorbates on Kr 36 by dotted lines. Taking the adsorbates obtained from aqueous solutions of Prop as a standard (pH ∿6), the influence of different additives, which may serve to enhance the adsorption is clearly seen. In the presence of a phosphate buffer (pH 6) the degradation rate remains on the same level as in pure aqueous solutions. Change of the pH to 7,6 by addition of NaOH accelerates the propantheline decomposition due to an increased concentration of catalytic OH ions. An unexpected low degradation rate is observed in the presence of $NaNO_3$.

Different effects may contribute to the better stability of Prop in the presence of this inorganic electrolyte. $NO_3^{\ominus}$ ions, counterions of $Prop^+$ as well as $Br^{\ominus}$ and $OH^{\ominus}$, may displace the catalytic active hydroxyl ions from the diffuse electrical double layer at the adsorbate-solution interface and, particularly, in the Stern layer of the adsorbate. It should also be considered that the amount of Prop adsorbed by hydrophobic interactions to

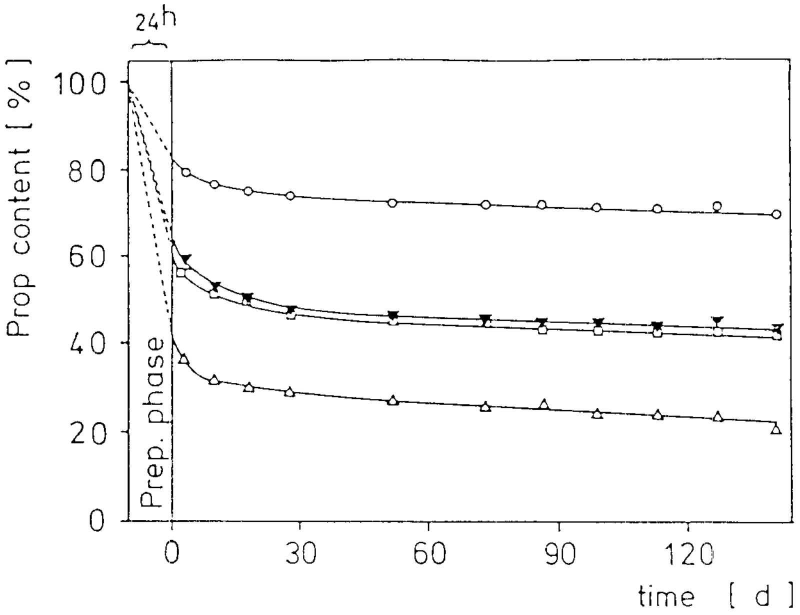


FIGURE 7

Hydrolysis of propantheline in adsorbates on Kr 36, prepared in the presence of different additives ($21^0C \pm 0,5$; 0% R.H.)

○ ——— ○ "Nitrate" - sorbate

▼ ——— ▼ "Water" - sorbate

□ ——— □ "Phosphate buffer" - sorbate

△ ——— △ "NaOH" - sorbate

the primarily-bound Prop cations is increased by the $NO_3^{\ominus}$ ions. These Prop ions are orientated to the aqueous phase and may be prevented from coming into close contact with the silica surface (7). This portion of the adsorbed Prop is, therefore, not available as a substrate for the catalytic action of silica surface groups.

After removing the adsorbates from the aqueous dispersion and drying them (in vacuo) they were stored over P_2O_5, corresponding to 0% R.H. at 21°C. A residue of 7% strongly adsorbed H_2O remains under these conditions in Kr 36-Prop adsorbates. Within the first three weeks of storage the hydrolysis of Prop in each of the adsorbates is characterized by an initial phase with high degradation rates, followed then by a period of an almost constant, considerably lower rate (full lines in Fig. 7).

At the beginning of the storage period the ratio 1:11 between adsorbed drug and water molecules on the silica surface is of the same order as discussed with ASA adsorbates.

At 0% R.H. there exists no supply of water for the hydrolysis of the drug from the gas phase. Water, which is consumed by the hydrolysis process must come to the sites of action - the ester group. This water transport becomes again the rate determining factor for the hydrolysis reaction, while the additives, very important in aqueous dispersions, are of minor importance here.

The degradation of Prop is accelerated if the adsorbates on silica are exposed to a storage climate with an increased rel. humidity (Fig. 8). Adsorbates prepared from pure aqueous solutions and from phosphate buffer are characterized by the same order of decomposition rate at 34% R.H. (dotted range Fig. 8 and R.H. >76%, hatched range Fig. 8). As expected in "NaOH" adsorbates higher degradation rates are observed (dotted lines), but the differences are smaller than in aqueous silica suspensions (7) and not so pronounced as in adsorbates of ASA on silica with the same content of NaOH. Adsor-

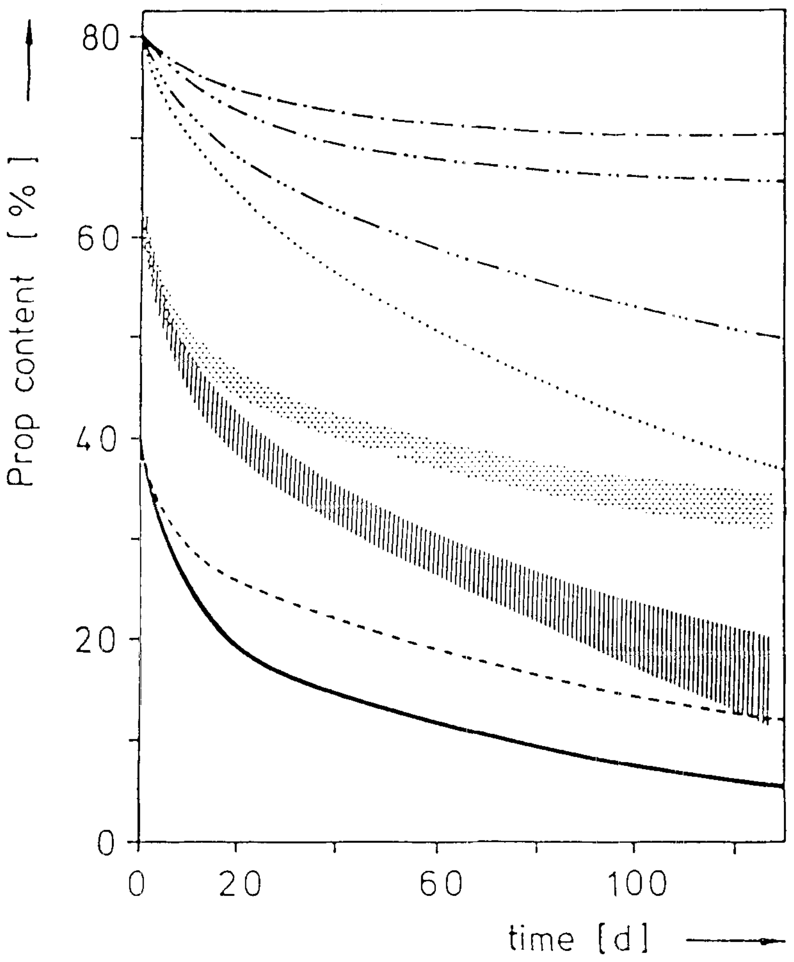


FIGURE 8

Propantheline hydrolysis in adsorbates on silica Kr 36. Influence of preparation (21°C ± 0,5).

░	34% R.H.	"water" and "phosphat buffer"	sorbate
▥	76-100% R.H.	"water" and "phosphat buffer"	sorbate
— — —	34% R.H.	"NaOH"	sorbate
━━━	76-100% R.H.	"NaOH"	
· — · — ·	0% R.H.		
·· — ·· — ··	34% R.H.		
··· — ··· — ···	76% R.H.		
· · · · · · · · · · ·	100% R.H.		

bates, prepared in the presence of $NaNO_3$ show the most substantial enhancement of the Prop hydrolysis rate if the R.H. is increased (Fig. 8 hatched-dotted lines).

Summarizing, the hydrolysis of Prop in silica adsorbates is characterized by the following features:

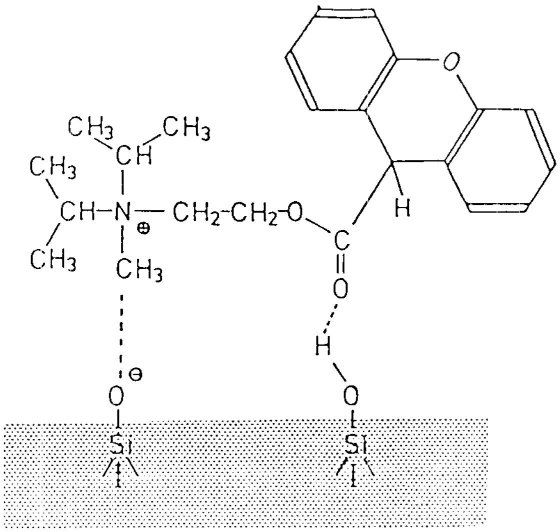
The decomposition rates are strongly dependent upon the relative humidities of the storage climate and, consequently, on the water content of the adsorbates. Transport of water to and on the surface is proposed to be the rate determining process.

From the specific degradation rates of the adsorbates found in the presence of different additives it seems apparent that Prop in direct contact with the silica surface decomposes faster than Prop adsorbed in the hemimicellar state, and therefore orientated with the polar groups to the aqueous phase.

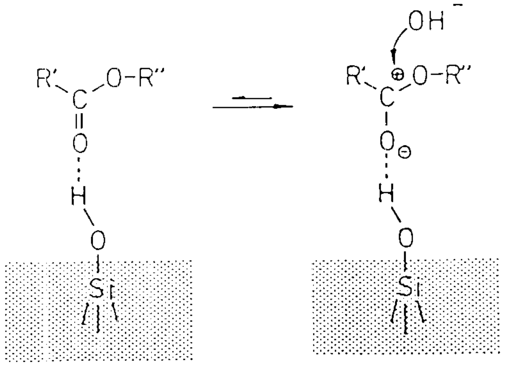
Compared to ASA adsorbates contaminated with alkaline impurities, the Prop adsorbates are not so sensitive to hydrolytic action upon the addition of NaOH.

From these results it is concluded that Prop cations are catalyzed in their hydrolysis by adsorptive interaction with the silica surface. Bound by the electrostatic forces between the quarternary ammonium groups and negatively charged adsorption sites on the silica surface they establish additional hydrogen bonds between the ester carbonyl groups and surface silanols (Fig. 9). This can be concluded from IR measurements of the adsorbates (17).

As a consequence the carbonium state of the ester linkage may be stabilized by these adsorptive interaction. In this way the



adsorbate structure



OH⁻ attack

FIGURE 9

Propantheline adsorbate on the silica surface: Interaction by electrostatic forces and hydrogen bonding; attack of the $OH^{\ominus}$ ion at the ester group attack of hydroxyl ions - the rate determining step of ester hydrolysis in aqueous solution (S_{N2}-reaction) - is facilitated (15). An increased number of dissoziated silanol groups at higher pH-values (after addition of NaOH) increases the number of ion exchange sites, but diminishes the number of silanol groups acting as proton donators for hydrogen bonding. This explains the relative intensitivity of the Prop adsorbates to alkali in comparison to ASA adsorbates. Adsorption in the presence of $NaNO_3$ means that most of the adsorbed Prop species are not in the correct position to allow these two adsorption mechanisms; they show better stability. In contrast to ASA, a desorption of the Prop at high water contents or in aqueous solutions is prevented by the electrostatic interaction, and, therefore, the total adsorptive state is not as sensitive to the water content of the adsorbates.

OXIDATIVE DEGRADATION

Butylhydroxyanisole (BHA)

The antoxidant BHA was chosen as a sensitive model for studying oxidative degradation in silica adsorbates. After reaction with oxygen dibenzofuran chinone is finally formed, with phenoxiradicals and a diphenol as intermediates (Fig. 10) (18,19). The loss of BHA was monitored by amperometric determination of the BHA content of the adsorbates (20).

In Fig. 11 the degradation of BHA in adsorbates on different silicas stored at 21°C and 37% R.H. are contrasted. With the excep-

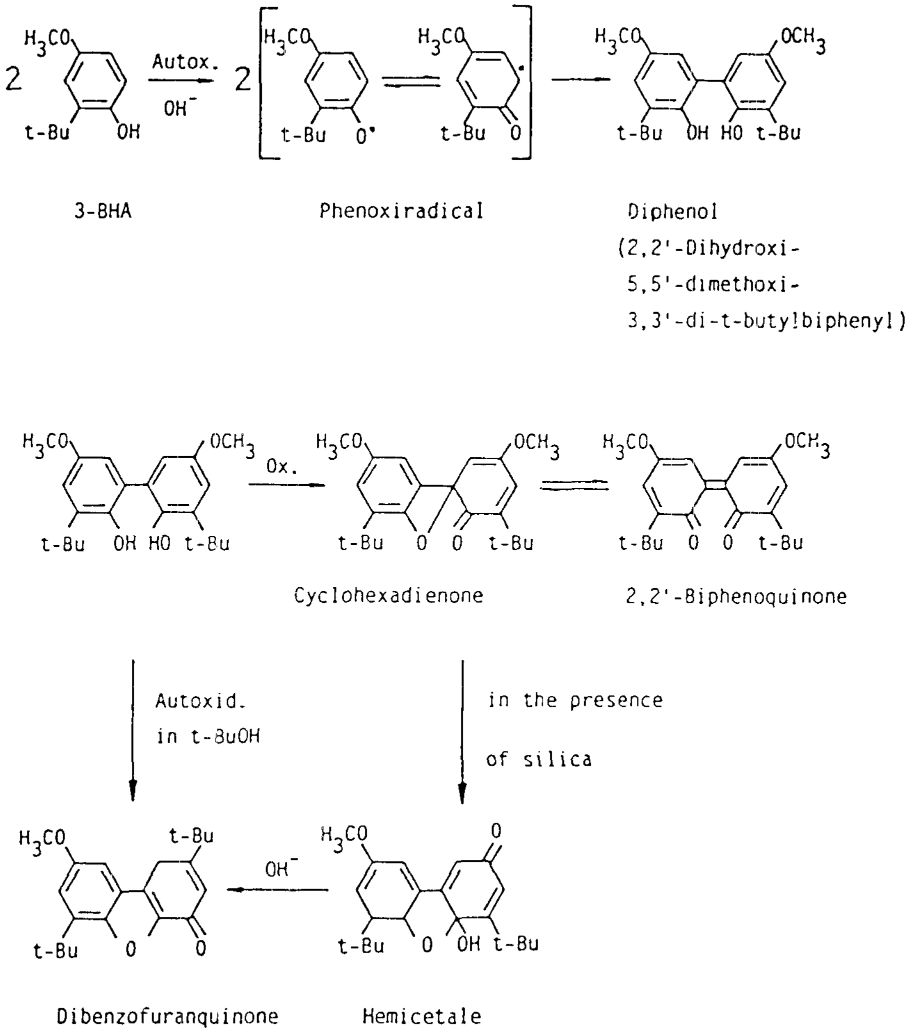


FIGURE 10

Course of 3-BHA degradation

tion of Syloid 244 the silicas do not significantly influence the oxidation of adsorbed BHA. Any catalytic effect of the silica surface can therefore be excluded. The different BHA stability in Syloid 244 adsorbates is attributed to the high content of impurities (Tab. 1) on the carrier, which act as catalysts in the oxidation process (21).

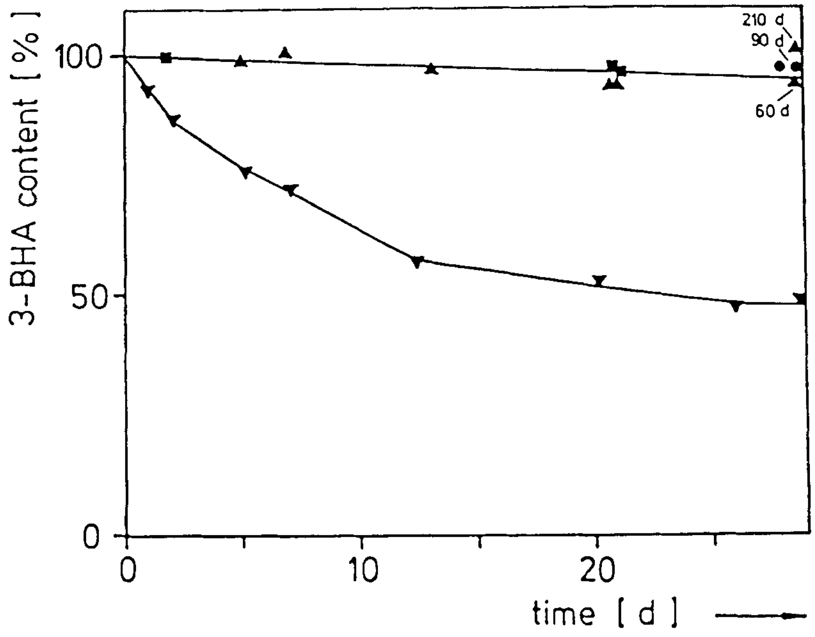


FIGURE 11

3-BHA degradation in adsorbates on different silica-carriers ($20^{o}C \pm 0,5$; 32% R.H.)

▲ —— ▲ A 200
■ —— ■ HDK N 20
▼ —— ▼ Syloid 244
● —— ● Kr 36

By increasing the R.H. an opposite effect is observed on "clean", low contaminated silicas and on Syloid 244. In adsorbates on colloidal A 200 and porous Kr 36 (both silicas with a low content of impurities), the oxidation is accelerated if R.H. values are established > 76% (Fig. 12). This can be explained by a progressive adsorption of the transport medium water on the surface.

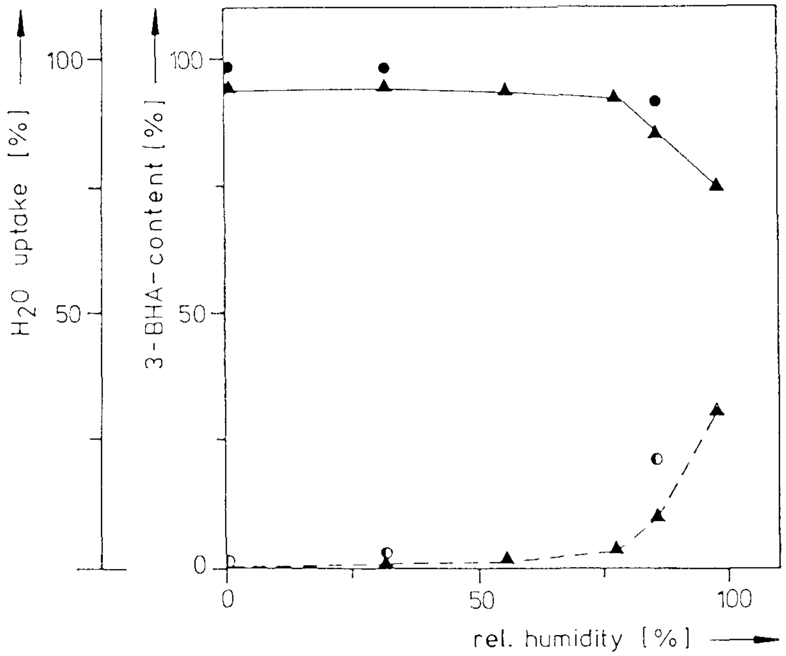


FIGURE 12

3-BHA degradation in SiO_2 adsorbates at different rel. humidities (20°C ± 0,5; $\theta = 0,5$).

●	Kr 36	3-BHA content after 86 d
◐	Kr 36	water uptake of the adsorbate
▲ —— ▲	A 200	3-BHA content after 86 d
▲ ---- ▲	A 200	water uptake of the adsorbate

On the Syloid 244 surface, however, increasing amounts of adsorbed water (corresponding R.H.> 80%) are accompanied by decreasing reaction rates for BHA oxidation (Fig. 13). The most outstanding difference in impurity content is the relatively high content of Al_2O_3. It is supposed that in the presence of higher amounts of water the surface-bound alumina may progressively act as Brönsted

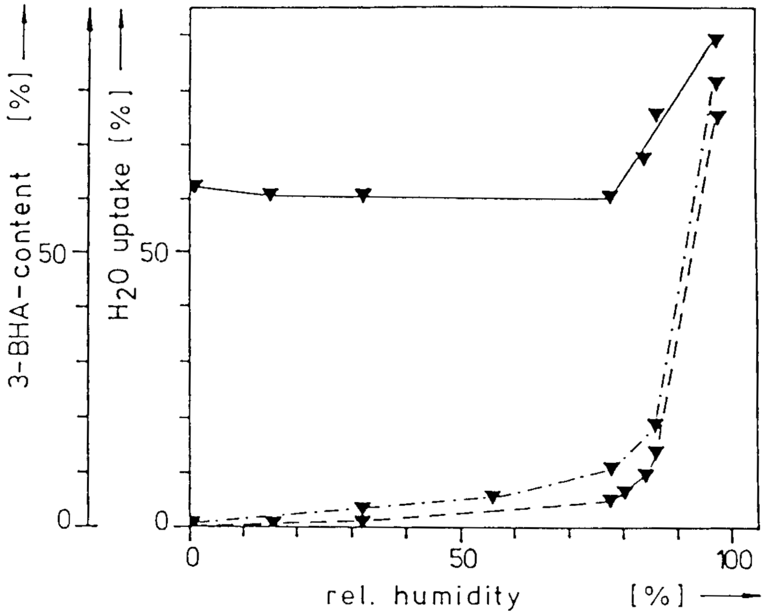


FIGURE 13

3-BHA degradation in Syloid 244 adsorbates at different rel. humidities (20°C ± 0,5; θ = 0,5).

▼ ——— ▼ 3-BHA content after 10 d
▼ ---- ▼ water uptake of the adsorbates (10 d)
▼ ·—·—· ▼ water uptake of pure Syloid 244 (10 d)

centres, generating H_3O^+ ions which reduce the surface pH in the adsorbates. Consequently, the stability of BHA is improved (20).

Linoleic acid methylester (LME)

In addition to the stability studies of different drug molecules on silica surfaces in dry adsorbates, the action of silica in contact with liquid LME should be outlined in brief.

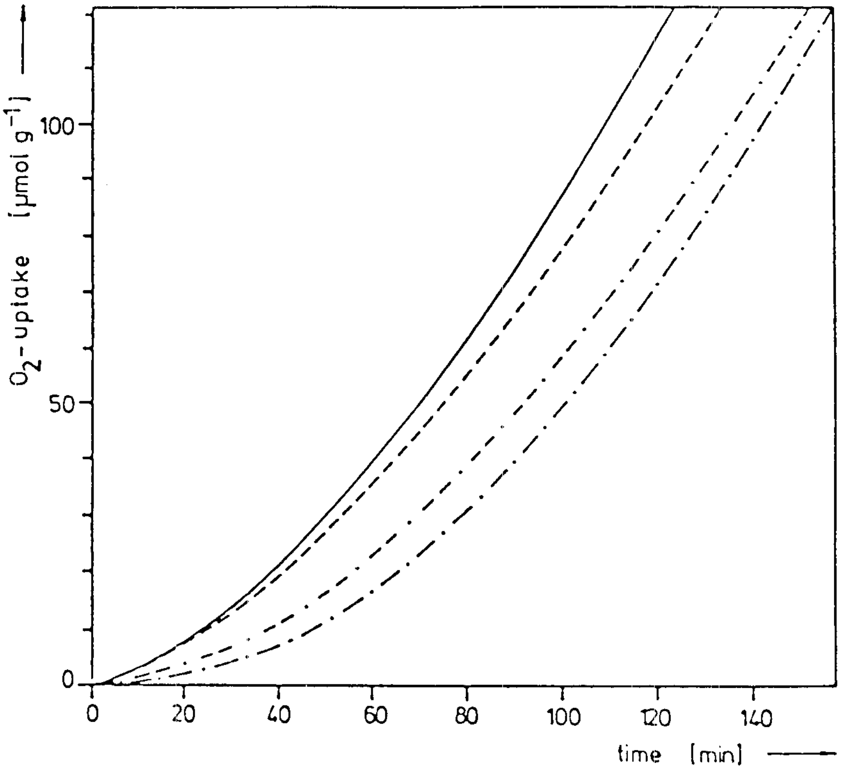


FIGURE 14

Oxygen uptake of linoleic acid methylester-SiO_2 (6%) dispersions during autoxidation, when exposed to UV-light (25°C ± 0,005; p_{O_2} = 213 mbar)

·—·—·—· LME
— — · — — · — LME Kr 36
- - - - - - - LME Syloid 244
———— LME A 200

Following the autoxidation of LME in suspensions of different silicas (6%) by measuring the oxygen consumption, characteristic differences are obtained (Fig. 14). The silicas are obviously promoting the autoxidation of the unsaturated compound, with the nonporous colloidal A 200 being the most effective catalyst, followed by Syloid 244 (with a high content of Fe_2O_3). Kr 36 exhibits the lowest catalytic action.

The enhancement of LME oxidation in the presence of silica is explained by adsorption of the reaction intermediates, the peroxides, onto the surface, which are then activated in the adsorbed state (20). Also taking into consideration the significant influence of metal impurities as catalysts, the different action of porous and nonporous silicas is obviously due to the slow transport processes inside the porous particles. This is in contrast to the rapid exchange of pro- and educts on the surfaces of the nonporous colloidal particles suspended in the liquid LME.

Summarizing the characteristic features of the oxidative or hydrolytic degradation of drugs in contact with the silica surface a different influence of the commercially available silicas on drug stability has to be considered.

Hydrolytic degradation is stimulated by basic as well as by acidic impurities, with the alkaline ones being the most effective by generating OH ions with adsorbed water.

The hydrolytic action of impurities is enhanced by increasing amounts of adsorbed water, which are dependent on the relative humidities of the storage climate.

Strong adsorption from aqueous media - i.e. by electrostatic interactions - provokes catalytic action of the silica surface on the hydrolysis of ester compounds by direct interactions between silanol groups and the ester groups. Molecules missing these strong electrostatic action are desorbed in aqueous dispersion from the silica and therefore a catalytic action is restricted to impurities, generating OH^- or H_3O^+.

Oxidative processes such as the phenol oxidation can also be stimulated by impurities, expecially by a combination of alkaline and heavy metal oxides.

Autoxidation of unsaturated compounds is catalyzed by an adsorption of the reaction intermediates, the peroxides, onto the silica surface.

The structure of the silicas - porous and nonporous - only influences the decomposition if the exchange of pro- and educts is necessary at the surface.

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