alcohol, and methyl alcohol. Needles were obtained which melted at 121.5–122°.

Anal. Calcd. for $C_{31}H_{50}O_2$: C, 81.88; H, 11.08. Found: C, 81.62; H, 10.90.

We wish to take this opportunity to express our thanks to the Rockefeller Foundation for a grant-in-aid for this work, to Merck & Co., Inc., of Rahway, New Jersey, for the analytical and absorption spectrum data and to Dr. O. H. Emerson of the University of California for kindly furnishing part of the crude sterol from wheat germ oil from which the α_1-sitosterol used in these experiments was isolated.

Summary

1. Certain experimental results on the determination of the structure of α_1-sitosterol are described.

2. An absorption spectrum study, and the non-formation of an addition compound with maleic anhydride, indicate that the two double bonds in α_1-sitosterol are not conjugated.

3. Only one of the double bonds in α_1-sitosteryl acetate can be hydrogenated under ordinary conditions. α_1-Dihydrositosterol and its acetate have been prepared and characterized. Evidence is offered to show that α_1-dihydrositosterol is an α-stenol.

4. The second double bond which is resistant to hydrogenation can be isomerized by dry hydrogen chloride into a position which is easy to hydrogenate. α_1-Isodihydrositosterol and its acetate have been prepared and characterized. Evidence is offered to show that α_1-isodihydrositosterol is a β-stenol.

5. Hydrogenation of α_1-isodihydrositosteryl acetate gives α_1-sitostanol acetate. Certain characteristic properties of this latter compound have also been described and we have observed that it may be obtained also by the direct complete hydrogenation of α_1-sitosteryl acetate at 65–70° in the presence of a small amount of concentrated hydrochloric acid.

6. α_1-Sitostanol and stigmastanol are not identical. This difference is probably the result of isomerization in the hydrocarbon side chain.

7. A structural formula for α_1-sitosterol has been proposed.

Electrolytes and the Viscosity of Pectin Solutions[1]

BY HUGO P. KORTSCHAK

Introduction

That the addition of electrolytes to certain colloidal solutions will cause marked changes in the viscosity is well known, but no explanation has been offered that seems completely satisfactory for all cases. This paper describes the effect of electrolytes on pectin sols, and shows that the colloidal character of the solutions is not a determining factor.

Experimental.—The pectin used was Eastman Citrus, practical. This was not the same sample used in the previous paper;[2] solutions prepared from it had a somewhat higher viscosity, indicating greater purity. The equivalent weight was 1500–2000. Other reagents were C. P. grade. Ordinary distilled water was used. No precautions were taken to prevent contamination by atmospheric carbon dioxide, except for boiling before use with substances containing calcium.

Since it is difficult to reproduce pectin sols exactly, a correction factor (always less than 2%) was applied to values at 0.1% pectin, to make them more easily comparable. Correction was made for density at salt concentrations above 0.1 N but no other correction factors were applied. For other experimental details see previous paper.[2] Viscosities reported are relative to water at the temperature of measurement, 27.5 ± 0.5°.

TABLE I

VISCOSITY OF 0.1% PECTIN SOLS

N added base	NaOH		Ca(OH)₂		KOH	NaOH + 0.001 N NaCl	
	η	pH	η	pH	η	η	pH
0	1.414	3.83	1.414	3.83	1.414	1.309	3.87
5×10^{-5}	1.424	3.93	1.419	3.82	1.434	1.323	4.00
1×10^{-4}	1.445	4.03	1.421	3.84	1.457	1.333	4.13
2×10^{-4}	1.474	4.32	1.428	3.91	1.504	1.339	4.52
5×10^{-4}	1.513	7.15	1.423	4.09	1.484	1.300	8.50
1×10^{-3a}	1.43	10.2	1.31	4.56	1.41	1.29	10.3
2×10^{-3a}	1.34	11.2	...	..	1.30	1.19	11.1
5×10^{-3a}	1.29	12.0	...	..	1.22	1.17	11.7

^{a} Pectin hydrolyzes rapidly in alkaline solution; viscosities at these concentrations are therefore inaccurate.

Discussion

It is evident that substances which increase the hydroxyl ion concentration raise the viscosity at low concentrations. Where the added substance is a strong base, as with sodium and potassium hydroxides, the maximum occurs when base and pectin are present in approximately equivalent concentration. This increase may be explained very simply. Pectin is an acid which is not completely ionized in the concentrations used. When neutralized with sodium hydroxide, the more highly ionized sodium salt is formed. If we admit that an increase in the electric charge causes increased hydration, and thus increased viscosity, the results are as would be expected.

A comparison of the viscosities of pectin and sodium–pectin sols supports this viewpoint (Table II). At great dilutions, where the acid would be largely dissociated, there is little difference between the two.

The increased viscosity at high salt concentrations is not, in most part, due to the presence of the pectin, as can be seen by a comparison between the viscosities of salt solutions with and without pectin (Table IV). Table V shows the behavior

TABLE II
DILUTION OF PECTIN AND NA-PECTIN

% P	η P	η NaP	Ratio
0	1.000	1.000	1.00
0.0016	1.016	1.016	1.00
.0031	1.033	1.031	1.00
.0062	1.066	1.059	0.99
.0125	1.106	1.104	1.00
.025	1.161	1.183	1.02
.05	1.260	1.302	1.03
.10	1.414	1.504	1.06

TABLE III
VISCOSITIES OF 0.1% PECTIN SOLS

N added salt	HCl	CaCl₂	KClO₄	Aconitic acid	NaCl + 0.005 N NaOH
0	1.414	1.414	1.414	1.414	1.476
2×10^{-5}	1.409	1.407	1.410	1.407	1.468
5×10^{-5}	1.406	1.399	1.405	1.402	1.457
1×10^{-4}	1.386	1.380	1.398	1.397	1.439
2×10^{-4}	1.353	1.352	1.380	1.381	1.426
5×10^{-4}	1.289	1.310	1.345	1.350	1.380
1×10^{-3}	1.263	1.284	1.313	1.315	1.339
2×10^{-3}	1.242	1.266	1.282	1.288	1.299
5×10^{-3}	1.235	1.254	1.253	1.258	1.267
1×10^{-2}	1.240	1.248	1.235	1.243	1.250
2×10^{-2}	1.237	1.248	1.223	1.233	1.236
5×10^{-2}	1.242	1.245	1.210	1.239	1.227
1×10^{-1}	1.246	1.256	1.203	·1.247	1.231
2×10^{-1}	1.255	1.275	1.189		1.238
5×10^{-1}		1.322			1.273

TABLE IVa
VISCOSITIES OF ELECTROLYTE SOLUTIONS WITH AND WITHOUT 0.1% PECTIN

N salt	KCl[a]	KCl + Pectin	NaCl[b]	NaCl + Pectin
0		1.414		1.414
1×10^{-5}		1.412		1.415
2×10^{-5}		1.410		1.414
5×10^{-5}		1.404		1.402
1×10^{-4}		1.391		1.398
2×10^{-4}		1.379		1.388
5×10^{-4}		1.340		1.351
1×10^{-3}		1.306		1.318
2×10^{-3}	1.000	1.277	1.000	1.282
5×10^{-3}	1.000	1.251	1.001	1.259
1×10^{-2}	1.000	1.241	1.002	1.243
2×10^{-2}	1.000	1.231	1.003	1.238
5×10^{-2}	1.000	1.222	1.005	1.232
1×10^{-1}	1.000	1.220	1.010	1.233
2×10^{-1}	0.999	1.216	1.019	1.236
5×10^{-1}	.998	1.211	1.046	1.276
1×10^{0}	.997	1.212	1.096	1.340
2×10^{0}	1.008	1.224	1.219	1.488

[a] G. Jones and S. K. Talley, THIS JOURNAL, **55**, 624, 4124 (1933). [b] G. Jones and S. M. Christian, *ibid.*, **59**, 484 (1937).

TABLE IVb
VISCOSITIES OF ELECTROLYTE SOLUTIONS WITH AND WITHOUT 0.1% PECTIN

N added salt	LiCl[c]	LiCl + pectin	NaNO₃[c]	NaNO₃ + pectin	Citric acid[d]	Citric acid + pectin[e]
0		1.414		1.414		1.414
1×10^{-5}		1.410		...		...
2×10^{-5}		1.408		1.405		1.413
5×10^{-5}		1.400		1.405		1.406
1×10^{-4}		1.400		1.387		1.399
2×10^{-4}		1.387		1.374		1.385
5×10^{-4}		1.359		1.343		1.355
1×10^{-3}		1.331		1.312		1.323
2×10^{-3}		1.301		1.287		1.286
5×10^{-3}		1.274		1.270		1.259
1×10^{-2}		1.257		1.259		1.242
2×10^{-2}		1.249		1.252		1.234
5×10^{-2}		1.243		1.243		1.234
1×10^{-1}	1.014	1.249	1.005	1.243	1.021	1.236
2×10^{-1}	1.028	1.260	1.010	1.249	1.039	1.255
5×10^{-1}	1.069	1.313	1.025	1.267	1.077	1.315
1×10^{0}	1.142	1.381	1.062	1.328	1.154	1.425

[c] "International Critical Tables." [d] Apparently not previously reported. At higher concentrations: 2 N, 1.330; 5 N, 2.23; 10 N, 7.4. [e] Note difference in quantitative values from those previously reported,[2] due to different pectin sample.

with varied pectin concentration. With higher salt concentration, a greater viscosity increase is to be noted in the series containing pectin than in the series of sodium chloride in water. Except for the most concentrated solution with 0.5% pectin, however, this effect is small when compared to the total viscosity increase, or to the viscosity decrease in more dilute solution. Some additional viscosity increase is to be expected

when pectin is present, since the pectin concentration, referred to water alone, is significantly greater in such concentrated salt solutions.

If the electric charge on the pectin micelle were reversed to any appreciable extent, one would expect the viscosity to remain at a value approximately that of a pectin sol containing no added electrolyte.

It is not suggested that the effect of the salt on water alone will suffice to explain all similar viscosity minima, but in some cases[3,4] the possibility apparently has not been considered.

The viscosity increase found here cannot be the same phenomenon as has been noted in the case of hydrophobic sols, for instance by Dhar.[5] In that case even potassium chloride produced an increase in viscosity, which is not the case here, and in all cases the rise commenced at salt concentrations which were far too low to give a measurable viscosity effect in water alone.

The decrease in viscosity which occurs at low salt concentrations is most probably due to a decrease in hydration.

From the data presented it can be seen that variation of the anion has no effect (with the exception of OH^-, due to the acid character of the pectin). Variation of the cation produces some change, but the minimum viscosity is nearly the same for all salts and acids.[6] The order of in-

TABLE V
VARIED PECTIN CONCENTRATION

N NaCl	0	% pectin 0.01	0.1	0.5
0	1.000	1.064	1.414	2.862
0.0001	1.000	1.040	1.398	
.0002	1.000	1.037	1.388	
.0005	1.000	1.030	1.351	
.001	1.000	1.025	1.318	2.781
.002	1.000	1.024	1.282	2.714
.005	1.001	1.023	1.259	2.679
.01	1.002	1.021	1.243	2.633
.02	1.003	1.023	1.238	2.601
.05	1.005	1.029	1.232	2.575
.1	1.010	1.030	1.233	2.580
.2	1.019	1.034	1.236	2.590
.5	1.046	1.067	1.276	2.676
1	1.096	1.113	1.340	2.736
2	1.219	1.236	1.488	3.116

(3) H. Erbring, Kolloid Z., 80, 20 (1937); C. A., 31, 6948 (1937).

(4) R. Haller and B. Frankfurt, Kolloid Z., 80, 68 (1937); C. A., 31, 6950 (1937).

(5) D. N. Chakravarti and N. R. Dhar, J. Phys. Chem., 29, 1556 (1925).

(6) That an amount of citrate equal in weight to the pectin present produced the solutions of minimum viscosity,[2] must be purely a coincidence, due to the ratio of the equivalent weights of the citrates and the pectin, and to the concentrations employed.

creasing effectiveness of the different cations follows the lyotropic series, Li, Na, K, Ca; the same order as is found, for instance, in solubility measurements.[7,8] This is the order of increasing hydration, and of increase in size of the ions.
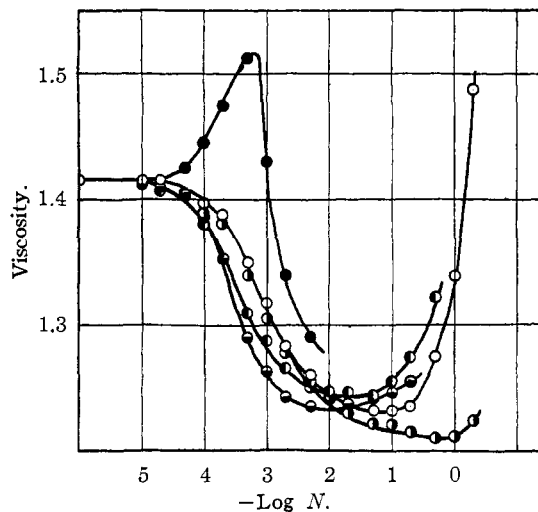

Fig. 1.—Viscosity of 0.1% pectin sols: ●, NaOH; ◕, HCl; ◑, CaCl₂; ◐, KCl; ○, NaCl.

Since the original purpose for which these measurements were made required only relative accuracy, no effort was made to obtain absolutely accurate values. For . this reason it seems unprofitable to apply the concept of activity, or, especially in view of the uncertain equivalent weight of pectin, to attempt a test of the applicability of the Debye–Hückel equation.

This decrease in viscosity conceivably could be due to any of several different influences: (1) A solvent effect, the pectin remaining unchanged except for loss · of water of hydration. In this case, the salt concentration required to produce minimum viscosity should be almost independent of the pectin concentration, which is not the case (see also the previous article). (2) Change in the acid dissociation of the pectin. The addition of electrolytes increases the dissociation constant of weak acids.[8] Also, the fact that the addition of alkalies will lower the viscosity, after a maximum has been reached, would make this explanation impossible. In view of the similarity of the curves for a strong acid, as hydrochloric acid, and for neutral salts, there can be no question of the effect being due to change in pH. (3) Adsorption

(7) H. v. Halban, G. Kortum and M. Seiler, Z. physik. Chem., A173, 449 (1935).

(8) H. v. Halban and H. P. Kortschak, Helv. Chim. Acta, 21, 392 (1938).

of ions, causing changes in the electric charge of the pectin micelle, or (4) the formation of undissociated salts of the pectin.[9]

These last two are very much the same thing, except that in the case of adsorption no definite limit to the amount of ion which can be adsorbed is to be expected, whereas with salt formation a definite limit exists, when the stoichiometric quantity of cation has combined with the pectin. It is this latter type of combination which seems to represent the facts most closely. Were more than an equivalent amount of cation to combine with the pectin, it would be expected that a considerable increase would occur in the viscosity. However, as has been pointed out above, no such large increase was found.

It is in accordance with this explanation, of the formation of an undissociated salt, that NaCl + NaOH, NaCl, CaCl₂, and HCl are progressively more effective in the order given. This agrees with the findings of Stuewer,[10] that calcium pectin is more highly dissociated than pectin itself, and sodium pectin still more so.

That the minimum ratio of electrolyte to pectin, which is necessary in order to attain the minimum viscosity, decreases with increasing pectin concentration (Table V), would be expected with both adsorption and salt formation.

When the viscosity has first been lowered with sodium chloride, subsequent addition of sodium hydroxide raises it only slightly (Table I), showing that there is less undissociated pectin acid present than in the absence of sodium chloride. The presence of additional ions does, of course, increase the dissociation constant of a weak acid,[8] which would account for this, but increased ionization appears to be associated with increased viscosity (see above). One must conclude that Na has replaced acid H in the pectin micelle (compare the conclusions of Rabinovich[11]).

Comparison of Pectin and Electrolyte Solutions.—The neutralization of an acid generally results in increased viscosity, i. e., a sodium chloride solution has a greater viscosity than an equivalent hydrochloric acid solution. Similarly, the viscosity of a pectin sol increases when the pectin is neutralized (Table I).

It has been noted previously that the viscosities of solutions containing two electrolytes are lower than would be expected on the assumption of a purely additive effect.[12] Since the viscosities of electrolyte solutions are low compared to those of equivalent pectin sols, an actual decrease in viscosity rarely has been noted, when a second salt has been added to an electrolyte solution. The data of Ruby and Kawai[12] show this effect when the measurements of 0.4 N hydrochloric acid solutions are examined (Table VI).

TABLE VI

VISCOSITY OF 0.4 N HYDROCHLORIC ACID (RUBY AND KAWAI)

c KCl	η	Calcd.
0[a]	1.0257	1.0257
0.1	1.0250	1.0260
.6	1.0221	1.0238
1.6	1.0285	1.0298

[a] Interpolated.

On the assumption that an electrolyte giving more viscous solutions than hydrochloric acid would show the effect more clearly, the data of Table VII were measured. (About ten measurements were made at each concentration, and the average reported. The average deviation of the individual measurements was 0.0015. Assuming statistical significance of the data, the probable error is less than 0.001 at each concentration.)

TABLE VII

VISCOSITY OF 1 N CITRIC ACID

c KCl	η	c KCl	η
0[a]	1.151	0.20	1.146
0.01	1.149	.50	1.147
.02	1.148	1.00	1.153
.05	1.148	2.00	1.183
.10	1.146		

[a] Interpolated.

It is evident that the behavior of citric acid is qualitatively similar to that of pectin. The viscosity is increased by 1 N potassium chloride, a concentration which decreases the viscosity of water. This would seem to be similar to the behavior of the more concentrated pectin sols (Table V).

Combination of some kind has been postulated in many papers reporting the conductivities of mixed electrolytes, whereas others use the "mixture rule" and its modifications.[13] It would seem that any satisfactory explanation must also account for the viscosity effects.

(9) By "undissociated salt" is meant only that the entire hydrated pectin micelle contains no excess of either positive or negative ions. To economize space, the well-known references to McBain, Loeb, Pauli, et al., will not be given here.

(10) R. F. Stuewer, J. Phys. Chem., **42**, 305 (1938).

(11) A. I. Rabinovich, Z. physik. Chem., **116**, 97 (1925); cf. C. A., **19** 3048 (1925).

(12) C. E. Ruby and J. Kawai, THIS JOURNAL, **48**, 1119 (1926).

(13) See, for instance, R. W. Bremner, T. G. Thompson and C. L. Utterback, THIS JOURNAL, **61**, 1222 (1939), and literature there cited.

Summary

1. The viscosity of pectin sols as affected by the addition of various electrolytes has been determined.

2. Three separate effects are present with increasing electrolyte concentrations: (a) An increase in viscosity at low electrolyte concentration, when an alkaline substance is added. This is due to the formation of the more highly ionized pectin salt from the pectin acid. (b) A decrease in viscosity to a minimum, further increase in electrolyte concentration having no apparent effect on the pectin. The formation of practically uncharged, undissociated salts of pectin is suggested, causing dehydration, and thus decreased viscosity. (c) Increase in viscosity at high salt concentration, due to interaction of the added electrolyte and water; an increase greater than this being due, in part at least, to the increased concentration of pectin with respect to water alone.

3. Any increase in viscosity which could be ascribed to reversal of charge on addition of excess electrolyte is either absent or very small.

4. The viscosities of solutions of pectin and of truly soluble electrolytes change in similar manner with increasing electrolyte concentration.

The Preparation of Acetyl-5-fluorosalicylic Acid

BY C. M. SUTER AND ARTHUR W. WESTON[1]

As a part of a program of preparing various aromatic fluorine compounds[2] for the purpose of determining their pharmacological properties, it has seemed of interest to synthesize 5-fluorosalicylic acid and its acetyl derivative (fluoroaspirin). 4-Fluorosalicylic acid (4-fluoro-2-hydroxybenzoic acid) was prepared some time ago by Hodgson and Nixon[3] but its physiological properties were not investigated.

5-Fluorosalicylic acid was prepared by carbonation of the Grignard reagent obtained from 2-bromo-4-fluorophenetole,[2] followed by deëthylation of the ethoxy acid by hydriodic acid. It was noted by Hodgson and Nixon[3] that while 4-methoxy-2-fluorobenzoic acid could not be demethylated, the 2-methoxy-4-fluoro isomer reacted readily with hydrogen iodide. It is evident from the behavior of 5-fluoro-2-ethoxybenzoic acid that the position of the fluorine has little effect upon the ease of dealkylation when the alkoxy group is ortho to carboxyl.

Preliminary data obtained in a comparison of the toxicity of the 5-fluorosalicylic acid and its acetyl derivative with the fluorine-free compounds[4] using white mice as test animals show that 5-fluorosalicylic acid is approximately twice as toxic as salicylic acid while the acetylfluoro acid is about 50% more toxic than aspirin. Although it has been reported[5] that 5-bromosalicylic acid is twice as effective against several types of bacteria as the chlorine compound, no experiments on animal toxicity have been carried out. 5-Chlorosalicylic acid has the same germicidal action as salicylic acid.

Experimental

2-Ethoxy-5-fluorobenzoic Acid.—A Grignard reagent was prepared using ethyl bromide as a starter from 35 g. (0.16 mole) of 2-bromo-4-fluorophenetole and 4 g. (0.17 mole) of magnesium and the ether solution dropped with stirring into a beaker containing 40 g. of crushed dry ice. After the excess carbon dioxide had evaporated, ice and dilute hydrochloric acid were added, the ether layer separated and the water again extracted with ether. The combined portions of ether were extracted several times with 10% sodium bicarbonate and the latter acidified. There resulted 19 g., a 64.5% yield, of a slightly yellow solid which after crystallization from dilute alcohol or a mixture of benzene and petroleum ether melted at 65.5–66.5°. The acid is soluble in benzene, alcohol, acetic acid and slightly soluble in carbon tetrachloride.

Anal. Calcd. for $C_9H_9O_3F$: neut. equiv., 184.1. Found: neut. equiv., 184.6.

5-Fluorosalicylic Acid.—The ethoxy compound was deëthylated by refluxing 17 g. with 150 ml. of hydriodic acid (d. 1.7) for ten hours. The white solid which separated as the reaction proceeded was filtered off on a sintered glass funnel. Dilution of the filtrate with water and extraction with ether gave only a little more product. 5-Fluoro-2-hydroxybenzoic acid crystallizes from water in fine white needles which melt at 178.5–179.5°. It is

(1) Sharp and Dohme Post-doctorate Fellow, 1938–1939.

(2) Suter, Lawson and Smith, THIS JOURNAL, 61, 161 (1939).

(3) Hodgson and Nixon, J. Chem. Soc., 1632 (1929).

(4) We are indebted to Dr. Maurice L. Moore, Research Laboratories of Sharp and Dohme, for these results.

(5) Rochaix and Pinet, Bull. sci. pharmacol., 34, 486 (1927).