EVALUATION OF TRAGACANTH AND TRAGACANTH MUCILAGES.*

BY ADLEY B. NICHOLS.[1]

During the revision of the National Formulary VI it became the writer's task to develop a formula for a jelly of ephedrine sulfate. Obviously, one of the first questions to be considered was how much tragacanth should be used. Using as controls several jellies which were on the market, a formula was developed for a preparation which seemed to closely simulate the general gel consistence of the available products. The tragacanth which was used in the experiments was labeled number one, which would have seemed to indicate that it would be of the first order.

VARIATION IN JELLY OF EPHEDRINE SULFATE.

When the formula calling for 2.7 per cent of tragacanth was published in the N. F. bulletins the response was indeed surprising. From one side came the request to "use more of the tragacanth." Another stated that the jelly "is about the same consistency as the '—' preparation," while from another source came the report that "the formula will not make a satisfactory product as it contains entirely too much tragacanth, making a very thick jelly." The latter individual suggested the formula which now appears in the N. F. It contains one per cent of tragacanth which makes the above comments all the more interesting.

Strangely enough, one of the first calls the writer received after the appearance of the N. F. was one complaining that the Jelly of Ephedrine Sulfate gave a liquid preparation, and other reports of a similar nature followed. Needless to say the answer apparently was to be found in the type of tragacanth employed.

With this rather unique background, experiments were undertaken to develop a method whereby an ephedrine jelly of the proper consistence could be prepared from any given lot of tragacanth. The nature of the work has been such that it is not yet possible to state the exact detail of such a procedure for ephedrine jelly itself. However, some extremely interesting results are available and it appears that a most sensitive evaluation of tragacanth and tragacanth mucilages is possible.

FALLING SPHERE TEST METHOD.

With the desire to develop a method which would be within the scope of practicability for the retail pharmacist, various standard viscosimeters were eliminated, while the possibility of using a falling weight seemed to offer an opportunity for development. Fortunately, just as work along this line was started, a reference to the identical idea was found in the work of Middleton in the *Quarterly Journal of Pharmacy and Pharmacology*, Vol. 9, pages 493 and 506 (1936). It was also discovered that the work of Middleton on the evaluation of tragacanth and tragacanth mucilage had been included in the British Codex of 1934 and, the data thus found, materially aided this project in many instances.

Briefly, tragacanth is evaluated by first carefully preparing mucilages of different known concentrations and basic uniformity throughout. Under stand-

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ardized conditions steel balls are timed as they fall through the mucilages for given distances and the results are plotted to give a curve from which it appears that mucilages of any specifications may be prepared. Comparison of curves also indicates the relative values of specific tragacanths.

Until experience has been gained with whole tragacanth, and always with the powdered drug, it is necessary first to prepare and test one or two trial mucilages to determine the general or rough value of the gum. For gums which would fall in the official class, this would consist in preparing for instance, a 1:50 and a 1:80 dilution. By reference to the typical curves the results of the preliminary test would place the tragacanth in an approximate position of value. Then a series of seven or eight dilutions are carefully prepared each different from the next by five units, thus: 1:50, 1:55, 1:60, 1:70, 1:75 and 1:80. If whole tragacanth is being used it is desirable to grind it sufficiently to make the individual portions representative of the entire lot, otherwise considerable variation may be experienced. On this same basis, not less than five Gm. of tragacanth and not less than 300 cc. of water seems desirable for the preparation of any mucilage. Needless to say, the tragacanth should be weighed upon a good balance and the water should be carefully measured, using a graduated cylinder or it might even be weighed if necessary.

The mucilages are started late in the afternoon, placed in liter-bottles to allow for agitation, shaken intermittently until the gel begins to form, automatically suspending the particles, then allowed to stand over night and again shaken as necessary to produce a uniform mixture comparatively free from lumps. A standard No. 3 Coors Porcelain Gooch crucible is set up in a liter suction flask fitted with a Walter crucible holder and suction is applied to the flask. A Richards' filter pump (aspirator) serves admirably for this purpose. The mucilage may be poured or shaken carefully into the crucible, or a Bailey crucible holder may be placed on the top of the crucible and the bottle inverted over this. By the latter procedure the mucilage is drawn from the bottle by suction. Care must be observed to empty completely the bottle, particularly any small remaining clumps, and all material should be forced through the crucible. The mucilage is then transferred to a beaker. If the mucilage is thin it will pour readily, but if it is thick the remaining traces should be scraped out. It is again drawn through the crucible and the process repeated at least a third time and as many more as required to produce a mucilage free from lumps and stringiness. The flask is then stoppered and the air is withdrawn completely by means of the vacuum pump. Violent agitation of the mucilage in the flask will help to clear the preparation toward the end of the operation after the vacuum has been applied for about ten minutes. Elimination of air bubbles is essential to obtain accurate reading. A portion of the mucilage is now poured carefully into a 25 mm. × 200 mm. test-tube to within about one inch of the top. Pyrex test-tubes seem to be desirable as they are of uniform diameter while some others which are available are found to be less than 25 mm. wide. Narrower tubes might have a constricting action on the speed of the ball. The tube which has been graduated previously to 10 cm. from a point about three cm. from the bottom of the tube, is stoppered and placed in a water-bath at 25° C. and kept there for one hour. It is then removed and suspended in a perpendicular position (suspension in a 100-cc. graduated cylinder was found to be most convenient). The cork is removed and another one, centrally fitted with a piece of glass tubing about seven or eight cm. long and having a bore of 5 mm., is inserted in such a manner that the tubing dips into the mucilage about one cm. A small slit should be made in the side of the cork to allow for expulsion of air.

One of the steel balls[1] (1/8 inch diameter, 0.130 Gm. in weight) is dropped into the centralizing tube and eventually passes into the mucilage proper. It will be noted that specifications for this tube and directions for its use have been given previously. The tube obviously insures that the consecutive balls will follow the same course which we will see is essential. By having the

[1] The balls used in these experiments were purchased from the Atlas Ball Co., Phila., Pa. Being high-grade bearings they run uniform in size and weight.

tube dip into the mucilage sufficiently the ball is checked in its initial fall and enters the mucilage proper free from any attached air bubble. If the mucilage is thin and the tube does not dip into it to the proper degree the ball will often carry an air globule with it, the latter retarding the fall of the ball through the measured column of mucilage. By placing the 10-cm. graduation near the bottom of the test-tube, sufficient space is allowed above the upper graduation to give the ball an opportunity to develop normal momentum before its speed is timed. The number of seconds required by the ball to travel 10 cm. is recorded, after which four or five additional balls are likewise timed.

It will be observed from Table I that the first ball always travels slower than those which follow, there being a marked difference between the time for the first and the second balls, with less variation between the second and third and those which follow. This explains the need for the centralizing tube which must be maintained in the same position until the tests have been completed. The path of the first ball apparently orients the colloidal particles of tragacanth along the central axis, thus making it easier for subsequent balls to follow. If a test on a certain mucilage is to be remade it becomes necessary to pour mucilage into another clean tube and not attempt to repeat the test upon the original tube. It is not even possible to run tests on an original tube on successive days without noting the above-mentioned effects of the first run of tests. When the tests are completed, the tubes are stoppered and then inverted to recover the steel balls. When subsequent tests were made even a day later, in this same material and tube, it was found that the speed of the ball reversed itself and instead of approaching a lower limit it approached a higher one. This was probably due to the particles being turned "inside out" when the tube was inverted for the removal of the balls. When the time for two successive balls does not differ by more than one or two per cent, the average of these two is taken as the final reading for that particular mucilage. Thin mucilage will show a greater degree of uniformity with fewer balls than will thick mucilage. It has not seemed necessary to use a constant temperature bath during the actual tests although it is desirable to perform the tests in a room as near 25° C. as possible. With heavy mucilage which may require up to ten minutes per ball, the possibility of any marked change in the temperature should be considered.

PLOTTING THE RESULTS.

When the time of fall of each dilution is plotted upon ordinary graph paper the result is a curve which is gradual, beginning with the high dilutions (thin mucilages) but rises abruptly with low dilutions (thick mucilages). Such a curve is difficult to use in this instance but by plotting the dilutions of the mucilage against the logs of the seconds of time of travel, the result appears to be a straight line, with

TABLE I.

Dilution of Tragacanth No. 12, 1 in ----	55.	60.	65.	70.	75.	80.	85.	90.
Time of Travel in Seconds	758	394	195.0	94.0	71.0	35.0	20.4	18.0
	615	342	166.0	80.0	60.0	29.5	18.0	15.5
	608	321	156.4	77.0	56.6	28.0	17.0	14.7
	...	310	?	75.0	55.7	26.8	16.0	14.3
	...	302	?	72.3	54.1	27.0	15.7	14.0
	...	299	145.0	72.1	54.6	...	15.5	14.0
Final Seconds	**610**	**300**	**145.0**	**72.2**	**54.5**	**27.0**	**15.6**	**14.0**

Complete results of tests upon several dilutions of a specimen of tragacanth.

the lines of various specimens approximately parallel. The range of operation is much greater and the accuracy of further estimated readings becomes much greater also.

TABLE II.—TIME IN SECONDS FOR BALL TO TRAVEL 10 CM. TEMP. 25° C.

Dilutions of Mucilage.	No. 12.	No. 13.	No. 14.	No. 15.
45	...	...	...	768.0
50	...	...	...	225.0
55	610.0	370.0	...	83.8
60	300.0	197.0	390	73.6
65	145.0	100.0	196	27.2
70	72.0	53.0	128	17.6
75	54.5	31.0	85	6.5
80	27.0	21.0	51	...
85	15.5	11.5	42	...
90	14.0	...	19	...

Final results of tests upon several dilutions of various tragacanths.

Table I shows the complete figures for a set of seven dilutions of one variety of tragacanth which were run simultaneously. Table II shows the final results of similar sets for four varieties of tragacanth.

In Fig. 1 are found the graphs which result when the figures of Table II are plotted as directed. It will be observed that the curve is of the straight line order and undoubtedly closer results would have been obtained, for instance, by grinding the tragacanth to even greater fineness,

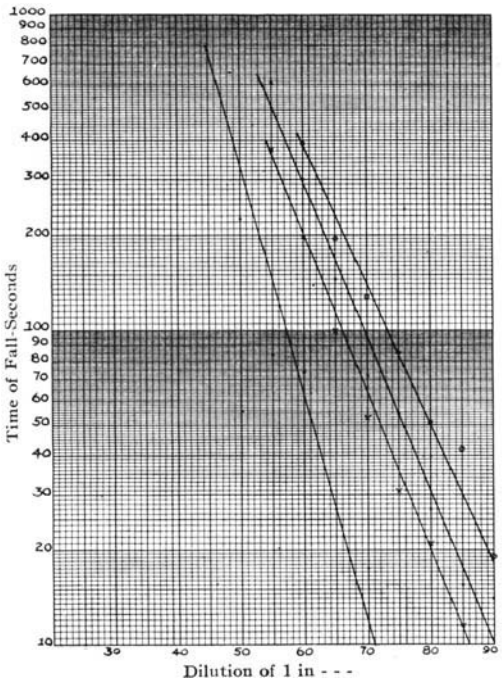

Fig. 1.—The curves from left to right are for tragacanths 15, 13, 12 and 14.

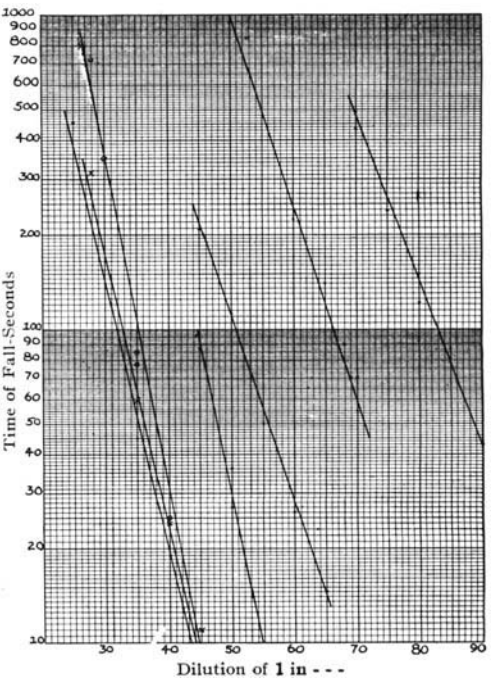

Fig. 2.—The curves from left to right are for tragacanths 2, 4, 11, 1, 8, 10 and 9.

the specimens in this case having been coarsely ground in a mortar without having made any attempt to specifically regulate the exact degree of fineness. From observations made throughout the work it is apparent that discrepancies occur when the whole pieces of tragacanth alone are

TABLE III.

Tragacanth Number.	Dilution 1 in - - - Rate of Travel in Seconds. 25.	28.	30.	35.	40.	45.	50.	55.	60.	65.	68.	69.	70.	75.	80.	81.	84.	85.	86.	90.
1						87.0	27	9												
							36	9.2												
2	−457			45.0	19/29° C.	8.8														
4		−316		59.5	24/26°	11.0														
8						209	112	50/26°	26	14.5										
													492	239	150					
9													432		95		47	87.0	69	43.0
															92					
															122/26°					
10							952		224	140/27°	90	70.5	55							
													71							
													70/26.5							
11		−720	350	85	25	9.3														
				78																
12							−2010		232?	192			130	57.7	27.0	27		15.5		14.0
									250?				107	54.5	29.5					16.4
									343				89							18.0
													72							19.0
13							−2340	370	197				37	31.0	21.0			11.5		6.0
									235	100			53		29.3					
14									390	193			119	85.0	46.0			42.0		27.3
									780				128		51.0					19.0
15						768	225	83.5	111.5	27.2			17.6	6.5						
							325		73.6				26.7							

Composite results of miscellaneous tests upon various specimens of tragacanth.

used. One portion may contain an exceptionally heavy piece which will produce a different mucilage than will the thin pieces; some tragacanths are made up of pieces of varying colors from white to yellow and each of these produces a different mucilage. Tests using larger quantities would obviate some of these differences also.

Figure 2 represents the composite results of tests, as also indicated in Table III, made at different times during the course of the experimental work. Some mucilages were prepared from whole tragacanths while other mucilages of the same specimen may have been prepared with the coarsely ground product. The laboratory temperature varied considerably on different days, and it is to be noted that the temperature at which a mucilage stands during the course of its preparation will cause a variation in the consistence of the mucilage. As an example, two mucilages of the same dilution were prepared, but one was made and stored at 25° C. while the other was held at 33° C. The former gave a reading of 63 seconds while the reading for the latter was found to be 88 seconds, which shows what a variation 7° will make. This factor may possibly need to be considered further. It will be observed that even in Fig. 2, composed as it is of a heterogeneous collection of data, the results still indicate curves of the straight line order.

TABLE IV.—IDENTITY OF TRAGACANTH SPECIMENS.

1. "Tragacanth A"—Whole—Wholesale Druggist No. 1.
2. "Powdered Tragacanth"—Manufacturing Pharmacist.
3. "Gum Tragacanth, No. 1 Flake"—Drug Importer No. 1.
4. "Tragacanth Gum, No. 1 Flake Powd."—Importer No. 1.
5. "Gum Tragacanth, No. 2 Flake"—Importer No. 1.
6. "Gum Tragacanth, No. 2 Flake Powd."—Importer No. 1.
7. "Gum Tragacanth, Aleppo Ribbon No. 4"—Importer No. 1.
8. "Gum Tragacanth, No. 4 Ribbon, Powd."—Importer No. 1.
9. "Gum Tragacanth, Ribbon, Extra Select"—Importer No. 1.
10. "Gum Tragacanth, Ribbon, Powd. Extra Select"—Importer No. 1.
11. "Powd. Tragacanth, No. 1."—Importer No. 1.
12. "Gum Tragacanth, Aleppo No. 1."—Jobber, Essential Oils, etc.
13. "Whole Tragacanth."—Drug Importer No. 1.
14. "Gum Tragacanth, Ribbon Aleppo No. 1—Whole U. S. P."—Drug Importer No. 1.
15. "Tragacanth A"—Whole—Wholesale Druggist No. 1.

TRAGACANTH EVALUATION.

An examination of the labels of the various tragacanths (Table IV) indicates that many of an inferior nature might be expected to be far more valuable than they actually are. The physical appearance of numbers 3, 5 and 7 would eliminate them from any such consideration for they obviously represent very poor grades of tragacanth. Knowing that 4, 6 and 8 are powders of these respective whole drugs would eliminate them at this time, but individually, of course, they look about alike in the powder form. Number 1 generally would be considered as satisfactory on its appearance and the source of number 2 would have acted as a voucher for it under normal conditions. Numbers 9 and 10 would be accepted without question, as would 11, 12, 13 and 14, although by physical comparison a difference in color might be noted as is the case in number 15, which contains many yellow pieces.

However, with the graphs of Figs. 1 and 2 available an entirely different story presents itself. It now would appear simple to interpret the relative value of each specimen of tragacanth in accordance with its placement upon the chart. One readily observes that numbers 2, 4 and 11 are poor products, and numbers 12, 13 and 14 are good varieties while number 9 actually would rank first.

A closer observation and study will give an actual numerical rating for each specimen based upon the dilution required for a certain number of seconds. If, for instance, 100 seconds is accepted as a standard, then number 2 tragacanth would be

required in a dilution of about 1 to 32 while number 8 would require a 1 to 51 dilution and number 9 would produce the same 100 second reading with a dilution of about 1 to 83. The actual ratings which might be given to these several specimens according to the falling sphere method appear in Table V.

TABLE V.

Tragacanth Number.	2.	4.	11.	1.	8.	15.	13.	10.	12.	14.	9.
Dilution 1 in - - - - for a 100 second reading	32	32½	35	45	51	56	65	66	69	73	83

Evaluation of Tragacanth Specimens.

U. S. P. TRAGACANTH.

Adoption by the U. S. P. of a method for tragacanth evaluation based upon this general procedure would seem wise in the light of the foregoing results. This would be in line with the British Codex which provides a time limit which a certain dilution of tragacanth must meet. It would appear from the above records that the U. S. P. might well expect a dilution of not less than 1 to 60 to produce a reading of 100 seconds. Such a test surely would advance the status of the U. S. P. monograph for tragacanth.

JELLY OF EPHEDRINE SULFATE.

Just as tragacanth itself might be judged and valued by a series of tests as described, so also it would seem quite possible to use these same results in the development of a uniform Jelly of Ephedrine Sulfate. Experiments along this line are now being conducted in the attempt to determine the "second" value for that tragacanth mucilage which seems to give a finished jelly of the proper consistence. Once such a record is established it should be simple, to again test an unknown tragacanth, plot the results and from the graph calculate the dilution which will give the desired mucilage, just as the dilutions in Table V would be expected to produce an approximate "second" value of 100.

TABLE VI.

Mucilage Number.	Reading in Seconds. 1st Day.	2nd Day.	4th Day.	5th Day.	13th Day.	35th Day.
1	56	64.5	75.6	76.5	104.0	136
2	28	31.0	34.6	35.2	48.6	68
3	...	16.2	18.5	18.8	25.5	37
4	140	...	203.0	...	...	400
5	...	70.5	83.0	...	111.0	...

Effect of age upon mucilage of tragacanth.

There are several additional factors which require consideration, however. Tragacanth mucilages become thicker upon aging as is indicated in Table VI. Heat, as we have noted, also increases the viscosity and both of these factors are being studied at present to determine the best possible solution to the problem of a uniform Jelly of Ephedrine Sulfate. Will it be practical to direct a given amount of heat to produce a maximum viscosity at once? Will it be practical to age the jelly for a given period of time? What will be the solution?

A further observation is that it would be desirable to strain the tragacanth mucilage at least through the Gooch crucible to assist in obtaining a smooth and

uniform jelly. Those who have some form of a colloid mill or homogenizer available will find that if the mucilage is processed by one of these units the resulting product will lose its characteristic granular or grainy appearance and will become perfectly smooth, adding materially to the appearance of the finished preparation.

CONCLUSIONS.

1. Jelly of Ephedrine Sulfate N. F. necessarily does not have the same viscosity when different specimens of tragacanth are used in preparing it.

2. Tragacanth U. S. P. varies to a marked degree in its mucilage qualifications.

3. A method is proposed whereby U. S. P. tragacanth would be required to pass a satisfactory mucilage test, based upon the time required for a steel ball to fall a given distance through a mucilage of definite concentration.

4. A Jelly of Ephedrine Sulfate of uniform viscosity may eventually be developed by using the falling ball method to determine the quantity of any given tragacanth to use in preparing the jelly.

MEDICAL ECONOMICS AND PHARMACY.*

BY R. T. LAKEY.[1]

In order that the best interests of the medical profession and of the public be served, all medical economics committees should be composed of carefully selected individuals appointed to represent each of the groups directly concerned in the costs of medical care. The nurse, dentist, clinical technician, social service worker and pharmacist are professionally related and interdependent. They all have a part in the proportionate distribution of the health dollar; therefore, a comprehensive consideration of health service economics, to be effective, must be inclusive rather than exclusive in character.

The medical profession is bound by a traditional code of ethics which prevents its members from undertaking for themselves and for their profession the dissemination of a type of propaganda which might help in correcting to a large extent professionally and socially dangerous trends.

The pharmacist is in a strategical position, because of his public contacts, to do a great deal of effective missionary work for the independent practice of medicine. That he has not done this in the past is partly the fault of the medical profession in not officially including him as a part of the professional family concerned with medical care. There is a sound psychological foundation for the belief that, had organized medicine given attention to its pharmaceutical needs, and had it exercised a certain amount of control relative to the development of educational standards and legislation affecting pharmaceutical practice, the drug store of to-day might be different. If he, the pharmacist, had been given proper recognition he might have developed professional pride and with it social consciousness to a greater extent. Without the advantages of such recognition, with its implied advice, guidance and coöperation, he has gone a long way in establishing for himself sub-

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