

Scientific Section

Papers Presented at the Sixty-Second Annual Convention

REPORT OF COMMITTEE ON QUALITY OF MEDICINAL PRODUCTS—AUGUST, 1914.

The Chairman waited until July 16th for the usual valuable contributions of the other members of the Committee, at which time that of Prof. Scoville was the only one obtained. As the Chairman was to leave on a vacation the 31st it became necessary to leave each other member to submit a separate report.

The continued activities under pure food and drug legislation are undoubtedly working toward better standards and greater carefulness, but there is still a tendency to allow the enforcement of regulations to become one-sided and work serious and uncalled for injustice. In the near future this will result in reaction or in the establishment of better methods on the part of the authorities.

There is no good reason why goods sampled should not be sampled in duplicate and the sealed duplicate be given to the person supplying the sample. In the event of the department official finding his sample defective, the holder of the sealed duplicate should have the privilege of having it examined by an experienced chemist to learn if the original report is correct, and the result of this examination be made known to the department official. This might do away with some very serious mishappenings such as have transpired in the past. It is stated that one firm of manufacturers was widely advertised as adulterators and a quantity of goods destroyed, when subsequent investigation proved that they were of standard quality, but the department chemist had made an error in placing his decimal point, so that the goods were ten times too weak on paper only. Some restitution should be made in such cases, without putting the sufferer to still more expense in an effort to secure justification.

In another instance the product of a manufacturer was condemned in a department publication. The statement was spread broadcast and placed in the hands of every physician in the state. The chemist of the manufacturer called upon the official chemist for an explanation, but received scant courtesy. Later the manufacturer received a statement that the goods had been re-examined and found 66%, 76% and 87% from the same analysis. The chemist of the manufacturer finally obtained permission to assay the same sample in the official laboratory under the immediate supervision of the Asst. Dept. Chemist. The analysis which was signed and certified as to accuracy by the Asst. Dept. Chemist, made the product 109%. No one was authorized to undo the damage to reputation and business but the sufferer himself.

Other instances could be cited where products were said to contain ingredients that were not present and could not have been present. Prof. LaWall in the Am. Druggist is quoted as saying—"A great deal of money has been wasted by the Government and a great deal of unnecessary expense has been entailed upon manufacturers by prosecution on trivial charges which if true involved on real damage to the cause of pure food and pure drugs. A prosecution based upon 4 percent deficiency in the alcoholic content of tincture of opium, though the morphine content was fully up to the standard, a ruling that the presence of one vetch seed in a million of coriander would necessitate the labeling of a sausage in which this was present as "containing leguminous starch," a ruling against a sample of cresol because it differed one decimal figure in the third or fourth place

from the requirements as to specific gravity, though exceeding those requirements in germicidal power, are instances of a kind of meticulousity which has no place in so serious a business as the enforcement of the food and drugs act."

An editorial in the July Am. Druggist calls attention to rulings and interpretations that seem to be far-fetched and unreasonable. It states—"It is not the law; it is the man who administers it that counts, and unfortunately too many of the officials who interpret, administer and try to enforce our laws relating to foods and drugs are theorists, not practical men. The graduate from a college put in charge of a state laboratory may be able to detect one part of salicylic acid in a million parts of strawberry jam, but unless he knows that salicylic acid is a normal constituent of many berries he may cause expensive trouble by over zeal. It might be a good idea to require at least one year's practical experience in a manufacturing laboratory, canning or preserving plant, as a requisite for appointment as analytical chemist in the public service." The most scrupulous and painstaking manufacturer may suffer from the inattention or misdoing of his employees but he should not be subjected to the injustice of being advertised for variations from the standard which do not exist.

Reports of various boards show that there is still remarkable variation in the strength of simple products as supplied by the retailer.

Spirit of Peppermint	1% to 80%	of official strength.
Tinct. of Iodine	56% to 89%	" " "
Spirit of Anise	9% to 81%	" " "
Spirit of Camphor	55% to 75%	" " "

but these cases of variation are comparatively few in number compared to the total number of samples examined. In some states the character of the balances, weights and measures in common use in drug stores is very severely condemned, a serious number being found defective.

Many lots of Oil of Birch and Oil of Wintergreen have been condemned as mixtures of Methyl Salicylate and other distillates. New tests have been published which claim to give the presence of such sophistications. One of these tests is 5 drops of a five percent solution of vanillin, 5 drops of suspected oil and 2 cc. C. P. concentrated Sulphuric Acid. With Methyl Salicylate a very pale green color results; with Oil of Birch a blood red, and with Oil of Gaultheria a deep crimson red. Another form of the test adds 1 cc. of alcohol. The use of drops is a gross inaccuracy to start with and all color reactions are of no value unless the absence of other bodies that might give similar reactions is first determined. With the wide range of organic matter an unknown, unexpected or unfamiliar vegetable principle may vitiate the test.

To determine its value the test was applied using the following materials.

ONE A 5% alcoholic solution of Vanillin.

TWO A mixture of pure Methyl Salicylate 300 parts and Oil Cedar Wood 1 part. This mixture gives the optical rotation and responds to the other pharmacopœial tests for true oil of Wintergreen Leaf.

THREE Pure Methyl Salicylate.

FOUR Oil of Birch guaranteed to be strictly pure by a dealer who does not market Oil of Wintergreen Leaf.

FIVE Sample of Oil of Birch guaranteed by a dealer to be pure to his certain knowledge.

SIX Oil of Birch from a prominent manufacturing chemist.

SEVEN Oil of Birch from a distiller guaranteed absolutely pure.

EIGHT Oil of Birch from a distiller guaranteed absolutely pure.

NINE Oil of Birch from a dealer who has assured himself by observation and tests that it is absolutely pure.

TEN Methyl Salicylate 99 parts, Oil Cedar Wood 1 part.

ELEVEN Oil Gaultheria Leaf from dealer who guarantees it absolutely pure from investigation of its source and by chemical examination.

TWELVE Oil Gaultheria Leaf from a distiller.

THIRTEEN Oil Gaultheria Leaf from a distiller.

FOURTEEN Oil Gaultheria Leaf from a dealer who has assured himself of reliability of source and has had it carefully examined for purity.

In applying the test 3 minims each of the Vanillin reagent and the oils were mixed with 2 cc. of C. P. Sulphuric Acid and the color noted on mixing (Column A.) After 17 hours color was noted (Column B.) One cc. of alcohol was added and color noted (Column C.) After 24 hours color was noted (Column D.) A separate test was made by mixing 1 cc. of each product with one cc. of C. P. Sulphuric Acid not using any Vanillin reagent with the oils (Column E).

TABLE

	A	B	C	D	E
1	Pale green.	No change.	No change.	Dark green.	Deep red soon changing to olive green.
2	Pale cherry or dark amber.	Little darker.	Deep crimson like No. 14.	Deep crimson	Very pale straw.
3	Pale green.	No change.	No change.	Dark green.	No color.
4	Deep cherry red.	Much darker inclining to crimson.	Deep violet red	Violet.	Deep blood red.
5	Deep cherry red.	Little darker.	Darker red.	Deep red.	Amber.
6	Amber only.	Little darker.	Some darker.	Deep red.	Pale Amber.
7	Amber only.	Little darker.	No violet.	Deep red.	Dark Amber.
8	Amber only.	Little darker.	No violet.	Deep red.	Amber.
9	Between No. 4 & No. 6	Little darker.	No violet.	Violet red.	Very pale Amber.
10	Darker red than 3, 6, 7 or 8.	Little darker.	Violet crimson red.	Deep crimson.	Straw color.
11	Deep cherry red.	Little darker.	More crimson.	Deep violet blue.	Deep blood red.
12	Amber red.	Little darker.	More crimson.	Violet red.	Light blood red.
13	Dark amber red.	Little darker.	More crimson.	Violet red.	Light blood red.
14	Deep crimson red.	Little darker.	Violet red.	Violet blue	Blood red

By studying this table it will be seen that No. 4 and No. 5 Birch Oil gave the deep cherry red with "A" test but No. 4 became very much darker and with "E" test gave a deep blood red while No. 5 gave amber only.

The mixtures of Cedar Wood Oil and Methyl Salicylate gave a good test for pure oils with test "A" but an entirely different and characteristic reaction with test "E." All but two of the birch oils would be rejected by tests "A," "C" and "E" yet were all specifically guaranteed to be pure. Is it not probable that the oils in their color giving contents vary by different methods and the varying amount of care used in distillation? Is a color test that can be so easily modified by the addition of other substances to be depended upon?

After standing 36 hours the mixture of equal parts of the sample and C. P Sulphuric Acid gave the following—

No. 2	Decided separation of Salicylic Acid.				
No. 3	Greater	"	"	"	"
No. 4	Moderate	"	"	"	"
No. 5	Slight	"	"	"	"
No. 6	Decided	"	"	"	"
No. 7	"	"	"	"	"
No. 8	"	"	"	"	"
No. 9	No apparent	"	"	"	"
No. 10	Decided	"	"	"	"
No. 11	Small	"	"	"	"
No. 12	Decided	"	"	"	"
No. 13	"	"	"	"	"
No. 14	Very little	"	"	"	"

Later on all gave a decided separation of Salicylic acid.

Martin I. Wilbert has accomplished a table reporting the examination of 10,524 samples, of which 3288 or 31.2% were rejected. He also presents an interesting table showing the wide variation in the active constituents of drugs.

	No. of samples	Minimum %	Maximum %
Belladonna leaves	144	0.175	0.563
Belladonna root	115	0.110	0.780
Guarana	41	3.720	5.160
Hydrastis	114	2.30	4.85
Hyoscyamus	120	0.043	0.234
Ipecac	253	1.240	2.750
Jalap	173	3.67	21.76
Stramonium	127	0.140	0.470

He also calls attention to deterioration caused by heat, by constituents of the air, by ferments, by micro-organisms and by combination with inorganic bodies.

Of 718 prescription balances examined in Kansas 195 were unfit for use, nearly one-half of the prescription weights were condemned. He states that tablets under most favorable conditions may vary from 10 to 30% from the quantities claimed.

In the Chemical Laboratory of the Am. Med. Association of 20 samples of 5 gr. Tablets of Potassium Iodide only two were below 94% of stated strength, one was 106.6% of stated strength, average 99.75%. Fl. Ext. of Goldenseal ranged in strength from 82% to 135% of official alkaloidal contents, while the declared alcohol contents varied from 40% to 66%. Nineteen samples of Morphine Sulphate T. T. ¼ gr. varied from 84.10% to 115.94% of stated strength, average 97.6%.

ACETANILIDE Tablets 5 gr. were 4.36 gr.

DEPT. AG.

ACETANILIDE COMP. Tablets contained 2.898 gr. Acetanilide instead of 3.5 gr. and 0.431 gr. of Caffeine Citrated instead of 0.5 gr.

DEPT. AG.

ACID CRESYLIC Varies considerably in color, solubility and in antiseptic value. Much of the commercial supply is below the U. S. P. standard.

W. L. SCOVILLE

- ADEPS LANÆ Sometimes contains sulphur compounds in appreciable amounts. W. L. SCOVILLE
- ALCOHOL Frequently 96% to 97% with objectionable amounts of non volatile matter. W. L. SCOVILLE
- Of 98 samples 47 or 47.9% were rejected. M. I. WILBERT
- ALOES One lot was free from Aloin. W. L. SCOVILLE
- ALUM DRIED 5% insoluble in water. Contained trace of iron, 7% water, was not clean.
- Lot 2, 3.5% water, 5.5% insol. in water.
- Lot 3, 2% water, 3.5% insol. in water. E. L. PATCH
- BEEF EXTRACT Varied from 7.4% to 17.88% salt. W. L. SCOVILLE
- BELLADONNA LEAF 0.3, 0.35, 0.099, 0.235, 0.30. E. L. PATCH.
- BENZOIN Six lots varied from 77% to 94% alcohol soluble matter. W. L. SCOVILLE
- BLACK HELLEBORE ROOT 15 lots Ash from 8.6% to 11.44%. Extractive from 22.3% to 31.6%. E. L. PATCH
- BLOODROOT Five lots yield 4.1% to 6% ether soluble alkaloids. W. L. SCOVILLE
- BORAX Of 17 samples labeled variously "borated skin soap," "real borax soap," "borax soap powder," etc., eight were free from borax, while others ranged from traces to 10%. J. IND. ENG. CHEM.
- CAFFEINE CITRATED TABLETS 2 gr. were less than 1 gr. DEPT. AG.
- CALOMEL TABLETS 2 gr. were .93 gr. DEPT. AG.
- CALOMEL & SODA T. T. 1 gr. Calomel were .62 grain.
- CANNABIS INDICA East Indian 10.1% Ether soluble resin to 12.2%. American consisted of leaves only. E. L. PATCH
- AM. CAN. IND. Tops contain 10% to 12% seeds and physically tests 80% of Bombay. SMITH, KLINE & FRENCH Co.
- CHLOROFORM Some lots contained chlorine compounds and organic bodies which modified the odor and made it unfit for use. W. L. SCOVILLE
- CINCHONA. RED 12 lots yielded from 7.21% to 11.63% total alkaloids. W. L. SCOVILLE
- COCHINEAL 10% ash including considerable magnetic iron oxide, Fe₃O₄. Had 75% of normal coloring power. Lot 2 5% ash, 75% of normal coloring power. Gray. Ash 5%, coloring power 100%. E. L. PATCH
- CRESOL
- Sp. gr. 1.029, Not soluble in 60 parts of water.
- Sp. gr. 1.038 Soluble in 90 parts of water insol. in 1 vol. 10% NaOH.
- Sp. gr. Soluble in 90 parts of water insol in 1 vol. 10% NaOH.
- Sp. gr. 1.028, Not soluble in 60 parts of water insol. in 1 vol. 10% NaOH.
- Sp. gr. 1.029, Not soluble in 60 parts of water insol. in 1 vol. 10% NaOH.
- Sp. gr. 1.036, Soluble in 60 parts of water soluble in 1 vol. 10% NaOH.
- Sp. gr. 1.030, Not soluble in 60 parts of water not soluble in 1 vol. 10% NaOH.
- Two out of six lots U. S. P. E. L. PATCH
- CUDBEAR Varies from 60% to 100% in coloring power. E. L. PATCH
- CUBEB Ran quite uniform the past year, yielding 18.1% to 22% oleoresin. W. L. SCOVILLE
- DAMIANA, PHOS. & NUX VOMICA TAB. 2-25 gr. Ext. Nux Vomica instead of ¼ gr. only a trace of phosphorus. DEPT. AG.
- DERMATOL Contained 20% of sulphur.
- GINGER ROOT Jamaica Ginger Ash 3.8%, Alc. Ext. 3.6% to 6.3%. E. L. PATCH
- GUAIAC RESIN Showed 67.5% to 92.8% soluble in alcohol. Four out of 8 lots were above 80% soluble. W. L. SCOVILLE

HYDROGEN PEROXIDE One lot contained arsenic in excess of 1 part in 100,000 and was deficient in strength. DEPT. AG.

HYOSCYAMUS Of 22 samples 2 were below 0.05%, two between 0.05% and 0.06%, six between 0.06 and 0.07%, five between 0.07% and 0.08%, three between 0.08% and 0.09%, two between 0.09% and 0.10% and two above 0.10%.

W. L. SCOVILLE

INFUSORIAL EARTH Much of that in the market contains carbonate or soluble matters which render it objectionable as a clarifying agent, unless washed with a dilute acid. W. L. SCOVILLE

IODINE TINCTURE 15 samples varied from 56% to 89%. MASS. B. H.

Of 984 samples 474 or 48.1% were not up to standard. M. I. WILBERT

IPECAC One sample of Rio contained 1.58% alkaloids. W. L. SCOVILLE

Rio 1.837%, Ash 5%, 2.12% alkaloid. Carthagea 1.818%, Ash 5.2%, alkaloid 2.4%, 2.13%, 2.4%, 2.29%. E. L. PATCH

IRON IODIDE Syrup labeled 10% contained 4.6%. DEPT. AG.

Of 549 samples 88 or 16% were rejected. M. I. WILBERT

JALAP Total resin 6.05% Ether soluble 0.9%

" " 9.67% " " 1.07%

" " 3.57% " " 0.72%

" " 8% " " 1.1%

" " 7.2% " " 0.9%

E. L. PATCH

KOLA 1.4% to 2.24% alkaloid. E. L. PATCH

One lot 1.6%. W. L. SCOVILLE

LEAD CARBONATE Was a mixture of Barium Sulphate and Sulphide.

E. L. PATCH

LARKSPUR SEED 1.12% to 1.76% alkaloid. E. L. PATCH

LUPULIN Is still in the market containing sand. One sample only 2.4% ash and three had 24%, 27.7% and 30.9% mineral matter respectively.

W. L. SCOVILLE

MACE Arillus of *Myristica malabarica*, false mace or Bombay Mace, worthless as a spice, used to adulterate and substitute the genuine mace, the dried arillus of *Myristica fragrans*. DEPT. AG.

CASTOR OIL Sold containing 33% of Cottonseed Oil. DEPT. AG.

OIL ANISE Lots answered all tests but that of optical rotation. They were guaranteed absolutely pure.

Opt. rotation + 0.4°

+ 0.4°

— 0.3°

+ 9.05°

Congealing point 6° C. (U. S. P. not below 15° C.)—1.0°

Congealing point 15° C. Sp. gr. 0.9796 —0.2°

Congealing point 15.5° C. Sp. gr. 0.9768 —0.2°

E. L. PATCH

OIL CLOVE Contained 15% of alcohol. DEPT. AG.

OIL CORIANDER Contained 20% Oil Caraway.. DEPT. AG.

OIL FENNEL Sp. gr. 0.9784 (U. S. P. 0.953 to 0.973) Congealing point 0° C. (U. S. P. not below 5° C.) N/D 1.5318 (22° C.) Opt. rotation + 14.5°. Was a Schimmel Oil guaranteed absolutely pure. E. L. PATCH

OIL LAVENDER (Mottet's) consisted of a mixture of Oil of Lavender and Glycerin esters. DEPT. AG.

OIL LEMON 14– 25 lb. coppers contained "washed Lemon Oil," the residue left after the pure Lemon Oil has been shaken with alcohol to make Lemon Extract, reinforced with Citral. DEPT. AG.

- OIL LINSEED Linseed Oil 50% Mineral Oil. DEPT. AG.
 Of 367 samples 138 or 37.6% were adulterated. M. I. WILBERT
- OIL ORANGE Sp. gr. 0.8458 N/D 1.473 (19.5° C.) Opt. Rotation + 89.5
 (U. S. P. not below + 95°.) E. L. PATCH
- OIL PEPPERMINT Odor fine. Taste good. Sp. gr. 0.9008. Opt. rotation
 —23.4°. Colorless 6.06 Menthyl Acetate, 47.58 total menthol. Odor inferior.
 Taste inferior. Sp. gr. 0.8925 (low) Opt. rotation—29.2°. 6.64% Menthyl
 Acetate, 50.74% total menthol. E. L. PATCH
- OIL OF TURPENTINE Different lots of Oil of Turpentine were grossly
 adulterated with mineral oil. DEPT. AG.
 Of 639 samples 132 or 20.6% were adulterated. M. I. WILBERT
- OLEORESIN CAPSICUM Insol. in ether. Only slightly soluble in alcohol.
 Nearly all soluble in water. Worthless as oleoresin. E. L. PATCH
- PAW PAW JUICE Dry, varies considerably in its digestive power. Of 47
 samples, eleven were below 50% of standard. Only 16 were acceptable, or about
 one in three. Some are adulterated with starch, but the proportion of starch does
 not correspond to their digestive power. W. L. SCOVILLE
- PEPPER BLACK Fruit of Piper longum substituted in whole or in part for
 that of Piper nigrum. DEPT. AG.
- PEPSIN Diluted with sugar instead of sugar of milk. Acid in powdered
 0.9% to 8%. In scale 6.8% to 7.6%. E. L. PATCH
- LIQUID PETROLATUM. Increased demand for an oil suitable for internal
 administration has brought oils possessing high physical qualities into the market.
 W. L. SCOVILLE
- SODA MINT TABLETS Lose both oil and ammonia. Standard makes
 titrated all right for Sodium Bicarbonate but gave 1-25 to 1-10 gr. Ammon. Carb.
 instead of ¼ grain, and 1-16 to ⅓ Oil Peppermint instead of ⅓ minim.
 E. L. PATCH
- SODIUM PHOSPHATE Has to be watched carefully for excess of
 Arsenic. Two lots were rejected for this reason. W. L. SCOVILLE
- SODIUM SALICYLATE Tablets 3 gr. were 1.82 gr DEPT. AG.
- SODIUM SULPHITE Crystal 77.62% Na₂ SO₃ 7 H₂O.
 " 96.07% "
 " 98.28% "
 " 68.23% " (marked 82%)
 " 22% " 78% Sulphate.
 Recryst. 46.95% "
 Crystal 87.4% "
 " 88.26% "
 Powdered 25% "
- DEPT. AG.
 E. L. PATCH
- SPIRIT PEPPERMINT Contained less than 1-10 of 1% of Oil of Pepper-
 mint and was deficient in alcohol. DEPT. AG.
 Fourteen samples varied from 1% of official to 82%. MASS. ST. B. OF H.
 Of 270 samples 139 or 51.4% were defective. M. I. WILBERT
- STRYCHNINE NITRATE T. T. 1-40 gr. were 1-70 gr. DEPT. AG.
- WORMSEED A large lot of unusual appearance and odor failed to yield
 any santonine. BULL. SCI. PHARMACOL.
- E. L. PATCH, Chairman of Com.

Memorandum:—In signing the report of the Committee on Quality of Medicinal Products, I desire to make several comments on statements contained therein.

1. I think that the evidence adduced to show that "there is still a tendency to allow the enforcement of the regulations to become one-sided and work serious

and uncalled for injustice," should be carefully investigated before being endorsed by the Committee or the Association. Such an investigation might show that the charges so recorded are based on *ex parte* statements, and are either without foundation or are seriously misrepresentative. Such unfounded charges are being systematically circulated, and in a way to appear sincere and truthful, thereby misleading the well-meaning. That the tendency above-quoted, exists, I am not denying, but I think that the greatest care should be taken in sifting specific charges, lest unjust conclusions should be drawn.

2. I think there must be some mistake about a Henbane that contained 0.234 percent of alkaloid. I think something else than the henbane must have been examined, probably Stramonium.

3. I think that something else than Belladonna leaf was examined when 0.099 percent of alkaloid was obtained, probably henbane. H. H. RUSBY.

Memorandum:—In signing this report I do not endorse the unverified charges made on pages one and two. The charges are rather serious and, if correct, should be verified by reference to publication or otherwise. Bald, general statements of this character can not be productive of good. I fully agree with the Chairman of the Committee that if anyone has been injured by error due to an inadvertence of the analyst, restitution to the fullest should be made. No manufacturer should be compelled to suffer loss of trade and be put to an expense as the cause of such error.

Respectfully,

L. F. KEBLER,

Chief, Drug Division, Bureau of Chemistry, U. S. Department
of Agriculture.

THE NEW SCIENCE OF IMMUNOLOGY.

F. E. STEWART, PH. G., M. D.

It is my purpose in this paper to call your attention to the new science of immunology on account of its rapidly growing importance to pharmacy. Biological products, as they are called, are products of immunization and they are used to produce artificial immunity for the prevention and cure of disease, and for diagnostic purposes. They are manufactured by the great pharmaceutical houses and also by physicians for their own use. They are already handled by the pharmacist, and as the new science of immunology develops, the demand for them will increase. Sooner or later, therefore, the science of immunology must occupy a more important place in relation to the educational work of the colleges of pharmacy, and text books must be written suitable for the use of pharmaceutical students.

Objections are strongly urged by some against teaching the science of immunology in colleges of pharmacy. It is said with some truth that the preliminary education of the pharmacist is not sufficient either in scope or character for him to comprehend it. Attention is called to the fact that the science of immunology deals with knowledge profound and complex, requiring a thorough medical education and post-graduate laboratory training for proficiency. The same objections might be as well urged against the teaching of chemistry in the pharmaceutical schools.

It is also objected that the practical application of the knowledge of immun-