scum is produced on the surface of the stain. At this point a precipitation occurs and the real staining takes place which takes from five to ten minutes. Next wash in distilled water for several minutes or until the thin parts of the specimen have acquired a yellowish tint. The differentiation may freqeuntly be brought out more plainly by washing longer.

If the blood-smear, as an example, stains a uniform deep-blue, distilled water will bring about a differentiation, removing the blue from the acidophilic parts, leaving them well stained with an eosin color.

The differentiation produced by this stain is as perfect as can be obtained by any of the eosinated methylene-blue combinations, and is being used with a great deal of success on blood-smears, demonstration of bacteria in cellular exudates, pus, etc.

DETERIORATION OF NITROGLYCERIN TABLETS.

J. R. RIPPETOE AND N. SMITH.

Although within the past five or six years several prominent pharmaceutical chemists have expressed the opinion that nitroglycerin tablets are a stable preparation, there are still some who believe in their instability and that the deterioration is chiefly due to volatilization.

In 1907, Bernegau[1] stated, that "the loss of nitroglycerin appears to be in the granulation process, and that the tablets themselves are fairly constant" and Dohme[2] in the same year stated "that observations made in his laboratory appear to indicate that tablets of nitroglycerin do not deteriorate perceptibly in course of time." In 1908, Gane and Webster[3] referred to "nitroglycerin as a stable compound" and Edmunds and Roth[4] find that "contrary to the common opinion, nitroglycerin tablets do not deteriorate greatly with age." Again 1909, Dohme[5] comments upon a "comprehensive investigation of the deterioration of the tablets, that disprove the claim that these tablets deteriorate rapidly" and very recently Vanderkleed[6] stated that "nitroglycerin tablets when properly made are to be classified among the more stable products, * * * and the tablets will remain unchanged or practically so, for a considerable length of time."

The last comment was in reply to an editorial article referring to the very unstable nature of nitroylcerin tablets due to loss by evaporation.

Until the phenoldisulphonic acid method was proposed by Scoville[8] and its modification by the Bureau of Chemistry,[9] and also the May method,[9] there was no very reliable method for accurately determining nitroglycerin in tablets. We have found the modified Scoville method to be a very practical and reliable method.

The purpose of this paper is to report the results of several experiments and while not covering a very long period or many samples, we believe the figures are quite sufficient to demonstrate the stable nature of nitroglycerin tablets.

Samples of 0.01 (1/100) and 0.02 (1/50) grain hypodermic tablets, which were assayed on April 12, 1912, having been made sometime previous, were set aside on a laboratory shelf in ordinary cork stoppered glass tubes of

about 100 each. These tablets were again assayed by the modified Scoville method on Nov. 12, 1913, with the results as shown in the following table.

	April 12, 1912	Nov. 12, 1913
0.02 grain	0.0150 gr.	0.0149 gr.
0.01 grain	0.0061 gr.	0.0057 gr.

These tablets while they were deficient in nitroglycerin when made show practically no loss during a period of 19 months.

A 10 percent solution of nitroglycerin (strength was not confirmed by analysis) was mixed with sugar of milk to give a nitroglycerin content of 5 percent. This mixture upon analysis was found to contain 4.13 percent of nitroglycerin. A quantity of hypodermic tablets was made up from this mixture using the theoretical amount based upon the above analysis to give a tablet assaying 0.01 grain. The tablets upon assaying were found to contain 0.0102 grain nitroglycerin. These tablets were hand made while a lot of tablet triturates, which were made from a granulation on a machine using the same quantities as above assayed 0.0093 grain nitroglycerin.

The hypodermic tablets were also assayed by extracting with ether, allowing the ether to evaporate spontaneously and drying in a vacuum desiccator, over sulphuric acid, and found to contain 0.0114 grain residue (nitroglycerin?) which residue when assayed by the modified Scoville method yielded 0.0095 grain per tablet.

A lot of 0.02 grain tablet triturates made in 1907 were assayed in October, 1907, by the ether extraction method and appeared to be of full strength, but as shown above, this method gives too high results, and the saponification method proposed some years ago gives still higher results.

Two bottles each containing about 100 of these 0.02 grain tablets, were set aside in a closet, one of the bottles being corked and the other having only a piece of muslin over the mouth of the bottle to exclude dust. These tablets were assayed in November, 1913, by the modified Scoville method after having been stored as stated above for six years with the following results.

Tablets in stoppered bottle	0.0130 grain
Tablets in unstoppered bottle	0.0040 grain

In all probability these tablets would not have assayed, by the modified Scoville method, much over 0.015 grain when made. (Compare assay tablets in first experiment April 12, 1912.)

Conclusions: It is apparent that nitroglycerin will volatilize in the process of making the tablets if the granulation is exposed for any length of time, but after compressing the tablets and storing in ordinary corked bottles very little deterioration takes place.

The tablets will lose in strength if exposed in unstoppered bottles, therefore containers that are not air tight such as card board boxes should not be used.

[1]Bernegau, Am. J. Pharm., 1907, 79, 555.
[2]Dohme, D. A., Apoth. Ztz., N. Y., 1907, '28, 133.
[3]Gane & Webster, Drug Topics, 1908, 23, 197.
[4]Edmunds and Roth, J. Am. M. Ass., 1908, 51, 2131.
[5]Dohme, Proc. M. Ph. A., 1909, 104.
All the foregoing references through Digest of Comments on the U. S. P. Hyg. Lab., Wash.
[6]Vanderkleed, Am. Drug., July, 1913, 240.
[7]Am. Drug., May, 1913, 148.
[8]Scoville, Am. J. Ph., 1911, 83, 359.
[9]Murray, Proc. A. O. A. C., 1911, 248.

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