THE EFFECT OF AGE ON THE RATE OF DISINTEGRATION OF MANUFACTURED MEDICINAL TABLETS.

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The effect of age on the rate of disintegration of manufactured medicinal tablets is an important subject for investigation since excessively retarded disintegration may reduce the efficacy of the tablets.

Other than the extensive investigation made by a Committee of the American Pharmaceutical Manufacturers' Association under the Chairmanship of Dr. C. S. Leonard (1), (2) there is practically a total dearth of published data on this subject. Using the methods of testing the rate of disintegration previously devised by the Committee on Project No. 1 of the American Pharmaceutical Manufacturers' Association (3) Dr. Leonard's Committee studied the effect of aging for 1 year on 30 different kinds of tablets most of which were suspected of "hardening" (that is, showing retarded disintegration) in time. In summarizing the work of his Committee Dr. Leonard found that all of the tablets, with the possible but doubtful exception of one, still retained their disintegration rate of classification as defined by the aforesaid "Committee on Project No. 1" after aging for one year.

As a contribution to the literature on this subject the effect of aging for 1 year on the rate of disintegration of 228 different kinds of medicinal tablets of various types was determined by the writer. Of this number 8 were hypodermic tablets, 137 were uncoated compressed tablets and 83 were coated compressed tablets and included tablets of all of the classes defined by the Committee on Project No. 1 (3) with the exception of Class No. 9. The methods of testing the rate of disintegration were those of the Committee on Project No. 1 (3) and the tablets were stored in cork-stoppered bottles in a dark closet during the aging period.

For convenience of expression the terms "hardened" and "softened" will be used in this article if the time required for disintegration at the end of the aging period was respectively longer or shorter than the initial disintegration time, although the degree of hardness of a tablet is not a criterion of its disintegration rate. In analyzing the results of the tests a tablet was arbitrarily considered to have "hardened" or "softened" if its final disintegration rate varied 25% or more from its initial disintegration rate; this figure of 25% variation being considered to be necessary to reconcile the variables represented by differences in duplicate determinations and variations in physical construction of individual tablets of the same batch. Furthermore, since the changes in disintegration time upon aging were usually only a matter of several minutes at most, a 25% variation figure was not considered excessive as a basis for deciding whether the tablets had "hardened" or "softened."

Summarizing the voluminous results it was found that 9.5% of the uncoated compressed tablets "hardened" and 10.2% "softened," each kind of tablet, however, remaining well within the disintegration limits of its class as defined by the "Committee on Project No. 1" (3) so that no practical loss of efficacy was suffered by the tablets chargeable to retarded disintegration upon aging. Of the coated compressed tablets it was found that 25.3% had "hardened" and 7.2% had "softened," and also as in the case of the uncoated compressed tablets, all remained well within the disintegration limits of their classes. None of the hypodermic tablets

showed a measurable change in disintegration rate upon aging. These results are in line with those of Leonard (2) who found that 37% of all of the tablets examined by his committee required a longer time for disintegration after aging for 1 year and 23% required a shorter time, all, however, with the possible but doubtful exception of one, still remaining within their respective disintegration rate classification as defined by the aforesaid "Committee on Project No. 1."

These results and those of Leonard (2) indicate that many tablets may show more rapid disintegration after aging rather than slower disintegration, which is contrary to the popular notion that newly made tablets are always more desirable in regard to rapidity of disintegration. Effort is constantly made by producers to guard against so-called "hardening" of tablets with age and market tablets have been observed which disintegrated spontaneously due to over-zealousness of the producer in guarding his product against "hardening" or in insuring initially rapid disintegration. The 228 kinds of tablets reported upon in this article were the products of a single manufacturer, did not constitute the total list of tablets put out by the manufacturer and were not selected for the tests but were taken for test successively as they happened to come up for manufacture. The balance of the list of tablets will be also tested and if the conclusions warranted to date require modification a second communication will be made. Since the tablets used in this work were the product of a single manufacturer this data does not establish the status of the general tablet market in respect to the effect of age on the rate of disintegration of tablets. However, these results are likely indicative, since they are in line with Leonard's results which represented the products of several producers, and are published with the view of encouraging similar investigations and reports which cannot but react to the benefit of the consumer of these products. The duty of the producer in this matter is pointed out by Leonard (2) as follows:

"..... the only way a manufacturer can find out if his product hardens, if he is concerned about it, is to conduct just such a test as we have here reported. Our Committee could not examine all varieties of tablets, that would be a Herculean task. All we could hope to do was to show the trend and point out the method. That our results were negative, in that they did not show serious hardening, speaks well for the products of the modern pharmaceutical manufacturer."

The corresponding duties of the jobber and retailer are also so ably stated by Dr. Leonard in his report (2) that they deserve re-stating herewith in the interest of wider distribution:

"As one year is usually the maximum time of storage of tablets on the stock and jobbers' shelves, this means that the manufacturer gets a satisfactory product into the retailer's hands. What the latter may do with it cannot be predicted. If he keeps it on his shelves for 5 years more, some products may seriously harden. But we do not feel warranted in continuing the work of the Committee for 5 years to tell him so. This is a problem for the Pharmaceutical Association.

"Deteriorations other than those of hardening, deteriorations of chemical nature which interfere with the pharmacodynamic action of some products, may be expected to occur in 5 years, and are more serious than any hardening. The problem of failure to move out retail stock in half a decade is a problem of economics and of medical psychology, and can best be dealt with by a policy of detail attention and return credits in cases of overstocking."

REFERENCES.

(1) Proceedings, A. P. M. A., 1932; (2) *Ibid.*, 1933; (3) *Ibid.*, 1930.

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