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Research Paper

Liquid Penetration Testing in Commercialized Tablets

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Abstract
Background: *Liquid penetration tests are mostly performed in the research stage of formulation design of tablet, but the author reports the results of liquid penetration tests on commercially available tablets.*
Methods: *The rate of liquid penetration was measured in two ways: by measuring the time required for a given amount (10μl) of liquid to be completely absorbed into the tablet (test 1), and by measuring the relationship between the amount of liquid absorbed by the tablet and the elapsed time (test 2). The liquids used in the penetration tests were ethyl acetoacetate and water.*
Results and Discussion: *The variation in weight and thickness of Tablets A, B, C, and D used in (test 1) was small, with the coefficient of variation being approximately 1% or less. In contrast, the coefficient of variation in liquid absorption time was large, at 10-20%. A significant positive correlation was observed between the absorption time and the tablet weight/thickness ratio for each product, and it was confirmed that the liquid absorption time increases as the tablet weight/thickness ratio increases. The liquid absorption time of the Tablet A-old product was clearly shorter than that of new product. The shorter liquid absorption time of the older Tablet A products may suggest a change in the pore structure due to moisture absorption. In the ethyl acetoacetate penetration into Tablet A (test 2), square of permeated volume: V^2 vs. elapsed time: t plot and Log V vs. Log t plot showed a good linearity, and slopes of regression line of Log V vs. Log t plot was approximately 0.5. suggesting that the penetration of ethyl acetoacetate follows the Washburn equation. On the other hand, for the penetration of water into tablets A and B, the V^2 vs. t plot did not show linearity, but the Log V vs. Log t plot showed good linearity, and the slope of the regression line was much greater than 0.5. This suggests that the permeation of water into tablets A and B caused a significant change in the pore structure due to swelling. Furthermore, the intercept of the regression line of the Log V vs. Log t plot of the water permeability of tablet B showed a significant negative correlation with the tablet weight. The intercept of the regression line, Log t = 0, is the permeation volume at t = 1 (seconds). This suggests that for tablets with an almost constant volume, the weight fluctuation of the filling particles has a significant effect on the tablet's bulk density, and therefore on its porosity and initial permeation rate.*
Conclusion: *The method attempted by the author is simple and will be useful for analyzing the disintegration and internal structure of commercially available tablets.*

Key words: *liquid penetration test, tablet, Washburn equation, swelling*

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I. Introduction

Tablet disintegration begins with the penetration of liquid into the tablet, and the aggregated particles in the tablet exposed to the liquid change to a disintegrated state. Therefore, the rate at which liquid penetrates into the tablet has a significant effect on tablet disintegration. Liquid penetration tests are mostly performed in the research stage of formulation design of tablet [1-5], but the author reports the results of liquid penetration tests on commercially available tablets.

II. Methods

1. Experimental Design

The rate of liquid penetration was measured in two ways: by measuring the time required for a given amount (10µl) of liquid to be completely absorbed into the tablet (Liquid penetration test 1, Figure 1), and by measuring the relationship between the amount of liquid absorbed by the tablet and the elapsed time (Liquid penetration test 2, Figure 2) The liquids used in the penetration tests were ethyl acetoacetate (bp; 181°C, d; 1.021 at 25°C) and water, and the liquid temperatures were both 20°C.

The weight of the tablet was measured using a direct reading balance (0.1 mg), and the thickness was measured using a thickness gauge (0.01 mm).

2. Statistical analysis

Correlation analysis was conducted to determine factors related to liquid penetration into tablets. A value of $p < 0.05$ was considered statistically significant.

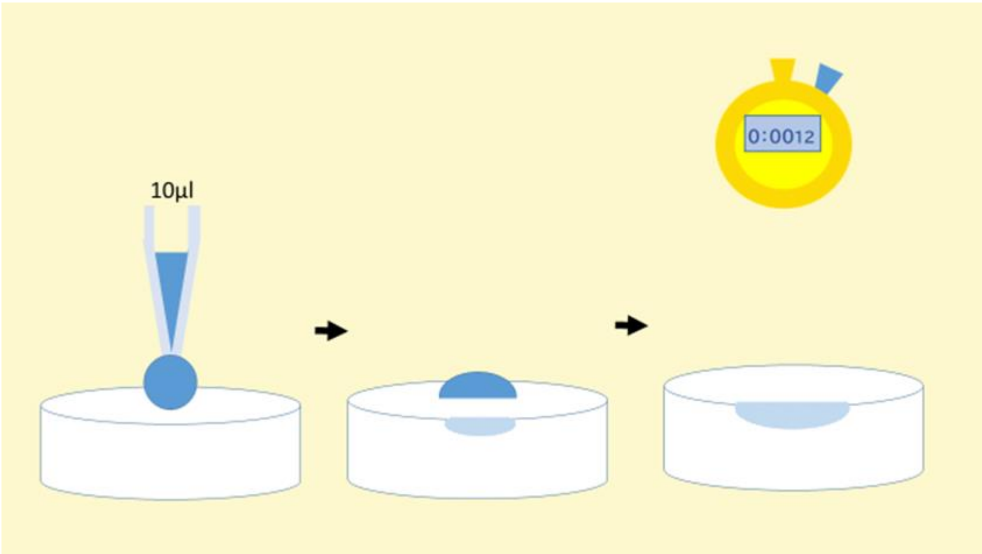

Figure 1. Liquid penetration test 2; Measurement of the time required for 10µl of liquid to be completely absorbed into the tablet.

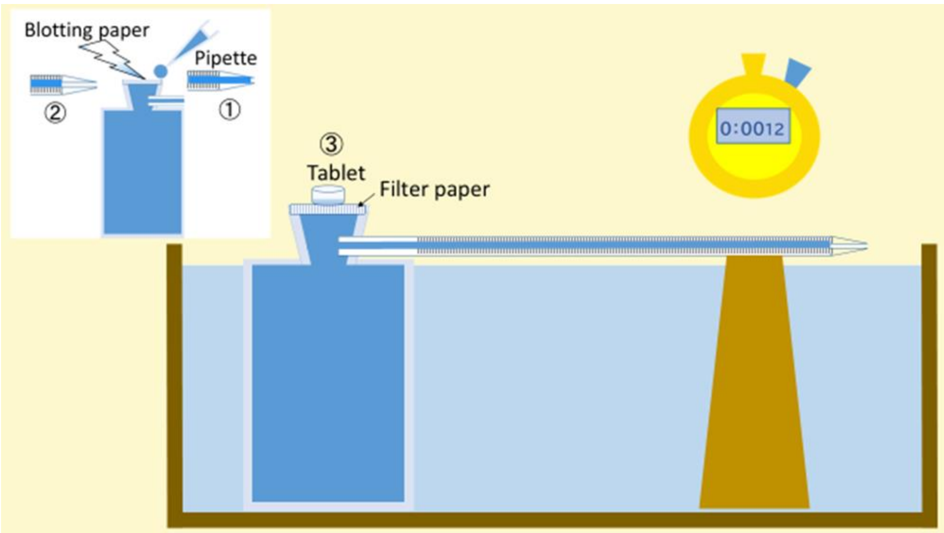

Figure 2. Liquid penetration test 1; Measurement of the relationship between the amount of liquid absorbed by the tablet and required time.

III. Results and Discussion

1. Liquid penetration test 1: Measurement of the time for liquid 10μl completely absorbed in a tablet.

Table 1 shows the weight, thickness, and liquid absorption time of the commercially available tablets used in test 1. The variation in the weight and thickness of each tablet was within 1% in terms of the coefficient of variation, which was slight, but the coefficient of variation in the liquid absorption time was large at 10-20%. Figure 3 plots the absorption time of ethyl acetoacetate and the tablet weight/thickness ratio for the newly purchased Tablet A and Tablet A (old product) purchased two years ago. A significant positive correlation was observed between the absorption time and the tablet weight/thickness ratio for each product, and it was confirmed that the liquid absorption time increases as the tablet weight/thickness ratio increases. The liquid absorption time of the old product was also clearly shorter. Figure 4 shows the relationship between the water absorption time and the tablet weight/thickness ratio for Tablets B, C, and D. All tablets showed a significant positive correlation between the water absorption time and the tablet weight/thickness ratio. The tablet weight/thickness ratio reflects the bulk density of the tablet, so the larger the tablet weight/thickness ratio, the smaller the porosity and the smaller the capillary diameter. This is thought to slow the penetration of the liquid. In addition, in the permeation test of Tablet A, the liquid absorption time of the older product was clearly shorter. It has been pointed out that tablets containing methylcellulose may swell and expand in their pore structure due to moisture absorption during long-term storage [6], and there are concerns that the strength of the tablets may decrease [7]. The shorter liquid absorption time of the older Tablet A products may suggest a change in the pore structure due to moisture absorption.、

Table 1. Weight, thickness and liquid absorbing time of tested tablets

Tablet	n	Weight (mg)			Thickness (mm)			Liquid absorbing time (sec)			
		Mean	SD	CV %	Mean	SD	CV %	Mean	SD	CV %	Liquid
Tablet A	20	440.9	2.7	0.6	4.011	0.011	0.3	15.52	1.78	11.5	a
Tablet A (old product)	8	442.8	5.8	1.3	4.065	0.027	0.7	7.91	1.50	19.0	a
Tablet B	14	341.4	3.4	1.0	3.043	0.013	0.4	6.14	0.85	13.8	b
Tablet C	10	250.6	2.2	0.9	3.256	0.020	0.6	3.74	0.33	8.8	b
Tablet D	10	181.9	1.4	0.8	2.727	0.029	1.1	16.00	3.10	19.4	b

a: Ethyl acetoacetate, b: Water

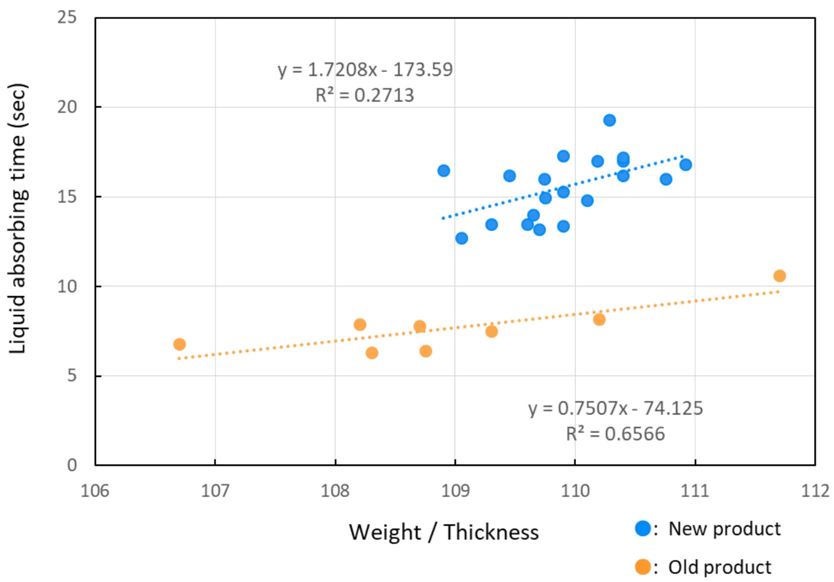

Figure 3. Weigight / thickness ratio vs ethyl acetoacetate absorbing time plots of Tablet A.

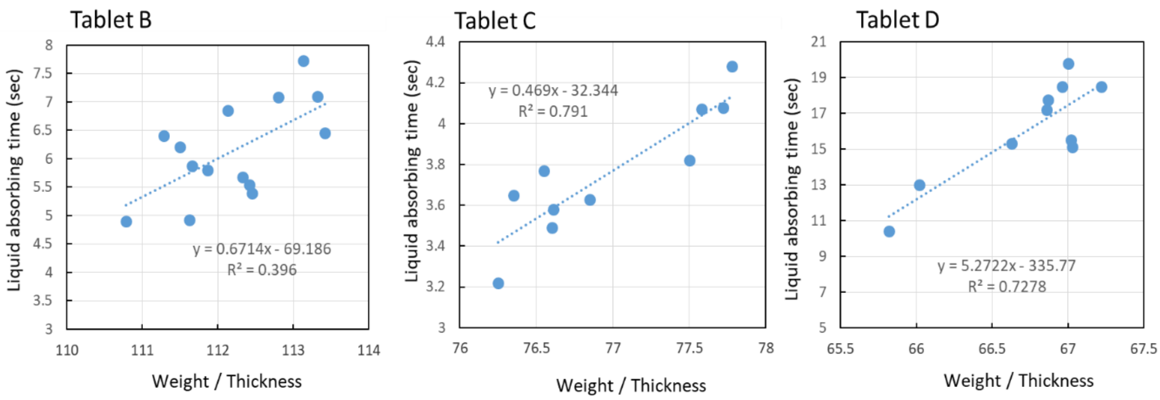

Figure 4. Weigight / thickness ratio vs. water absorbing time plots of Tablet B, C, D.

2. Liquid penetration test 2: Measurement of the relationship between the amount of liquid absorbed by the tablet and time.

The relationship between the amount of ethyl acetoacetate permeated into the Tablet A and the elapsed time is shown in Table 2 and Figure 4。 Square of permeated volume (V^2) vs elapsed time (t) plot and Log V vs. Log t plot in Figure 4 showed a good linearity, and slopes of regression line of Log V vs. Log t plots were approximately 0.5. On the other hand, water penetration into Tablet A did not show the linearity of the V^2 vs t plot, but Log V vs. Log t plot showed a good linearity, and the slope of regression line was much higher than 0.5 (Figure 6). The results of the water penetration test for 10 tablets of Tablet B are shown in Figure 7. Log V vs. Log t plot in Figure 7 showed a good linearity, and the slope of regression line was much higher than 0.5.
The penetration of liquid into the tablet capillaries follows Washburn's equation [8, 9]. Theoretically, it is expressed by equation (1).

$L^2 = R\ \gamma \cos\theta\ t / 2\ \eta$……………(1)

L: penetration distance, R: tablet capillary diameter, γ: liquid surface tension, η: liquid viscosity, θ: contact angle between the tablet inner wall and the liquid, t: time

If the tablet particles do not swell due to the penetration of the liquid, the capillary diameter does not change and the following relationship holds:

$V^2 = R\ \gamma \cos\theta\ t / 2\ \eta$……………(2)

V: Permeated volume

For the penetration of ethyl acetoacetate into tablet A, the V^2 vs. t plot and the Log V vs. Log t plot showed good linearity, and the slope of the regression line of the Log V vs. Log t plot was nearly 0.5, suggesting that the penetration of ethyl acetoacetate follows the Washburn equation. Tablet A may contain cellulose-based excipients. Non-polar solvents such as ethyl acetoacetate do not usually cause significant swelling in cellulose [10, 11]. On the other hand, for the penetration of water into tablets A and B, the V^2 vs. t plot did not show linearity, but the Log V vs. Log t plot showed good linearity, with the mean slope of the regression line (0.829 ± 0.052, n=10) much greater than 0.5. This suggests that the permeation of water into tablets A and B caused a significant change in the pore structure due to swelling. Furthermore, the intercept of the regression line of the Log V vs. Log t plot of the water permeability of tablet B showed a significant negative correlation with the tablet weight. The intercept of the regression line, Log t = 0, is the permeation volume at t = 1 (seconds). This suggests that for tablets with an almost constant volume, the weight fluctuation of the filling particles has a significant effect on the tablet's bulk density, and therefore on its porosity and initial permeation rate.

Table 2. Relation between of ethyl acetoacetate permeated into the Tablet A and elapsed time

Amount of ethyl acetoacetate permeated: V (µl)	Time required to absorb liquid (sec)			
	A-1	A-2	A-3	A-4
20.0	15.3	21.8	21.8	17.6
30.0	34.0	47.8	47.8	39.0
40.0	61.5	86.0	86.0	62.3
50.0	96.3	133.7	133.7	94.5
60.0	138.9	187.7	187.7	134.0
70.0	189.6	254.8	254.8	180.8
80.0	248.2	332.9	332.9	233,8
90.0	317.8	422.9	406.1	290.4
Total amount of ethyl acetoacetate permeated	104µl	95µl	97µl	103µl

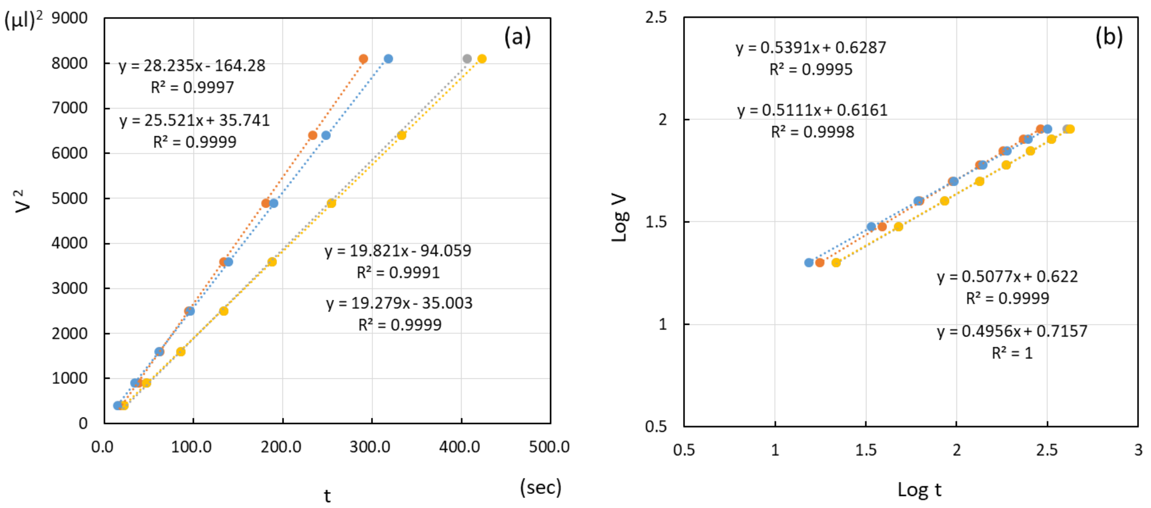

Figure 5. Square of permeated volume: V^2 vs. elapsed time: t plot (a) and Log V vs. Log t plot of the ethyl acetoacetate permeation into Tablet A (b). V: permeated volume (µl), t: time (seconds)

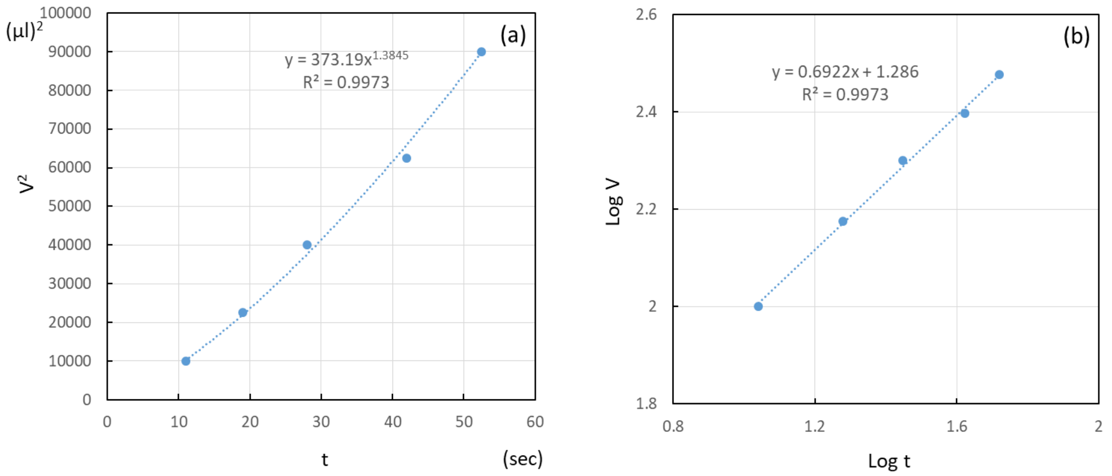

Figure 6. V^2 vs. t plot (a) and Log V vs. Log t plot (b) of water permeation into tablet A. V: amount of water permeated (μl), t: time (sec).

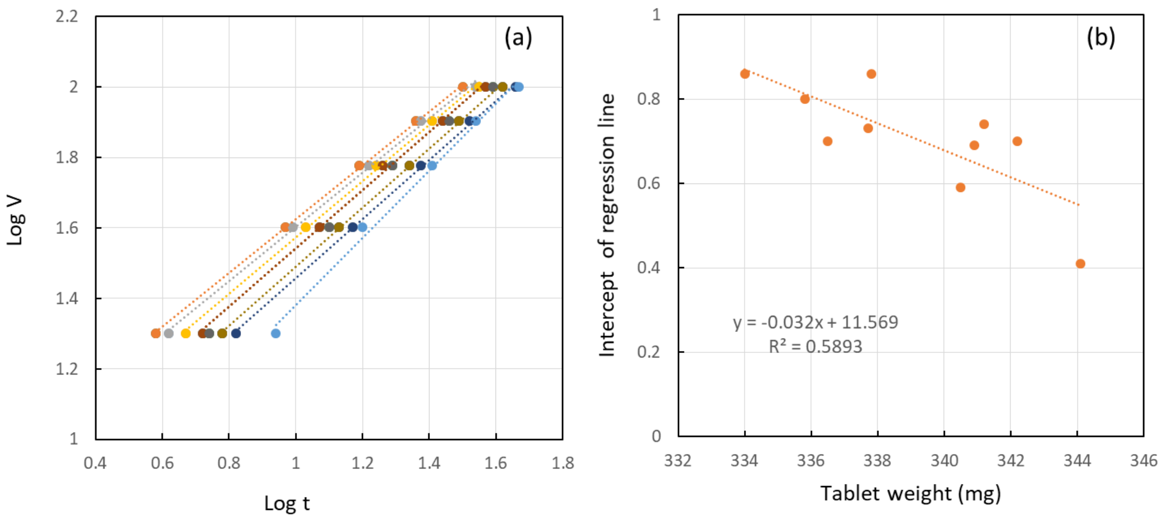

Figure 7. Log V vs. Log t plot of water permeation into tablet B (a) and the relationship between the intercept of the regression line and tablet weight (b). V: amount of water permeation (μl), t: time (sec).

IV. Conclusion

A liquid penetration test was conducted using commercially available tablets. With ethyl acetoacetate, penetration was observed according to the Washburn equation, and it was found that there was no change in the pore structure due to swelling. Furthermore, there were cases where the penetration rate was faster in older products, suggesting a change in the pore structure due to moisture absorption. Furthermore, in the water penetration test, the relationship between the amount of penetration and time did not follow the Washburn equation, suggesting a change in the pore structure due to swelling. The method attempted by the author in this study is simple and will be useful for analyzing the disintegration and internal structure of commercially available tablets.

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Disclosure of conflict of interest: The author declares that have no conflict of interest.

REFFERENCES

[1]. Jan Lenz, Jan Henrik Finke, Heike Bunjes, Arno Kwade, Michael Juhnke. Tablet formulation development focusing on the functional behaviour of water uptake and swelling. Int J Pharm X. 2021 Nov 2;3:100103. doi: 10.1016/j.ijpx.2021.100103

[2]. Daniel Markl and J.Axel Zeitler. A Review of disintegration mechanisms and measurement techniques. Pharm Res. 2017; 34:890–917. DOI10.1007/s11095-017-2129-z

[3]. Weiyong Li, Abraham Woldu, Lola Araba, Denita Winstead. Determination of water penetration and drug concentration profiles in HPMC-based matrix tablets by near infrared chemical imaging. Journal of Pharmaceutical Sciences. 2010; 99 (7): 3081-3088. doi: 10.1002/jps.22084.

[4]. D. Braido, Y. Gulak and A. Cuitino. Solvent penetration rate in tablet measurement using video image processing. AAPS PharmSciTech, Vol. 13, No. 2, June 2012 (# 2012). DOI: 10.1208/s12249-012-9769-4

[5]. Makoto Otsuka, Mitsuyo Sato and Yoshihisa Matsuda. Comparative evaluation of tableting compression behaviors by methods of internal and external lubricant addition: inhibition of enzymatic activity of trypsin preparation by using external lubricant addition during the tableting compression process. AAPS PharmSci.2001; 3 (3): E20. doi: 10.1208/ps030320.

[6]. Natalie Maclean, Ibrahim Khadra, James Mann, Helen Williams, Alexander Abbott, Heather Mead, Daniel Markl. Investigating the role of excipients on the physical stability of directly compressed tablets. Int J Pharm X. 2021 Dec 9:4:100106. doi: 10.1016/j.ijpx.2021.100106.

[7]. F. Kiekens, R. Zelko and J. P. Remon. Effect of the storage conditions on the tensile strength of tablets in relation to the enthalpy relaxation of the binder. Pharmaceutical Research. 2000; 17, No. 4, 491-493.

[8]. Edward W. Washburn (1921). "The Dynamics of Capillary Flow". Physical Review. 17 (3): 273. doi:10.1103/PhysRev.17.273

[9]. Lucas, R. (1918). "Ueber das Zeitgesetz des Kapillaren Aufstiegs von Flussigkeiten". Kolloid Z. 23: 15. doi:10.1007/bf01461107

[10]. Akari Okugawa, Yoshiaki Yuguchi, Chihiro Yamane. Relaxation phenomenon and swelling behavior of regenerated cellulose fibers affected by organic solvents. Carbohydrate Polymers. Volume 259, 1 May 2021, 117656

[11]. Ludmila C. Fidale, Naiara Ruiz, Thomas Heinze, Omar A. El Seoud. Cellulose Swelling by Aprotic and Protic Solvents: What are the Similarities and Differences? Macromolecular Chemistry and Physics. 2008; 209(12): 1240 - 1254. DOI:10.1002/macp.200800021