SPECTROPHOTOMETRIC DETERMINATION OF TOTAL FLAVONOIDS IN TAXA OF GENERA THYMUS L. (Lamiaceae)

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SUMMARY: Spectrophotometric method for determination of total flavonoids in taxa of genera Thymus L. is suggested. The method is based on the reaction of flavonoids with NaOH and forming the yellow coloured product that provokes bathochromic shift in UV spectra of flavonoids. Compensation spectra of plant flavonoids with NaOH, recorded against the solution without addition of NaOH, showed maximum absorption at 390 nm. Compensation spectra of apigenin in presence of NaOH showed maximum absorption at the same wavelength. Molar absorption coefficient of apigenin in the presence of NaOH was ε_k=24600 $mol^{-1}dm^3cm^{-1}$. The suggested procedure was checked by method of standard additions and recovery was between 99.2 % and 103.4 %. The content of total flavonoids determined in twenty-three samples, range from 0.53-2.59% and RSD is 1.43-11.3%.

KeyWords: Thymus, Flavonoids, Content determination, Spectrophotometry

Determination of total flavonoids in a particular plant or some other preparation on plant basis, could be done by using different analytical techniques: spectrophotometry, fluorimetiy, gas chromatography and high pressure liquid chromatography [1]. Spectrophotometric determination of total flavonoids is mostly based on forming complexes between flavonoids and a particular metal ion added in an alcohol solution of flavonoids. Created complex provokes the bathochromic shift in flavonoid UV spectra. As a reagents for making complexes could be used different metal salts [1-12]. Most of the data are concerned with $AlCl_3$, as reagent, dissolved in different solvents as water, methanol, ethanol or chloroform, prepared in different concentration, varying from 0.1-10 % [1, 9-12]. Besides the methods based on forming complexes between flavonoids and the different metal ions, total flavonoids could be determined spectrophotometricaly by using some other reactions of flavonoids like that with reducing reagents, reaction with diazonium salts and reaction with alkaline hydroxides [13].

Generally, for all mentioned methods for spectrophotometrical determination of total flavonoids is that neither of mentioned reagents isn't selective enough to react with all flavonoid contents in plant extracts and not to react in the same time with other phenol components presented in the plant extracts. Probably, it is necessary for every separate plant species to check the reproducibility of the results obtained by using some of the methods and if the one is not appropriate it will need modification of the methods or using a new one suitable for the certain plant material.

A lot of data point at obvious presence of the flavonoid contents in different taxa of the genera Thymus. Most of the data are concerned with isolation of separate flavonoids and their identification by certain structural examination [14-22] as well as chromatographic separation, identification and quantification of the flavonoid components [23, 24]. However, there is no data for spectrophotometric determination of total flavonoids in the taxa of genera Thyrnus L. in the available literature. The aim of this work is to establish a spectrophotometric method for determination of total flavonoids in taxa of genera Thymus.

Material and methods

Twenty three samples that belong to eleven different Thymus taxa, were collected from different places in Republic of Macedonia. Air-dried material was packed in paper bags and stored at dry and cool place. The identity of the taxa was confirmed by Dr. Matevski from the Institute of Biology, Faculty of Science from Skopje (Macedonia). The vouchers were deposited at the Herbarium of the same Institute of Biology, Skopje.

Reagents and instruments

Apigenin (Roth, Karlsruhe, Germany), 0.5 mol/L water solution of NaOH. All reagents that were used were of analytical grade. UV/VIS Spectrophotometer Perkin-Elmer model Lambda 16 was used for spectrophotometric measurements.

Preparation of methanol plant extract

Methanol plant extract was prepared by extraction of a small amount of milled plant material with mixture of ethanol:water (70:30 v/v) by heat-

ing on boiling water-bath. After cooling and filtration it was submitted to hydrolysis with 10 % solution of chloride acid. Than, the mixture was extracted with ethyl acetate and small volume of ethyl acetate extract was diluted with methanol. The last obtained solution was used for recording the absorption spectra of plant flavonoids.

Preparation of extracts for establishing of appropriate extraction agent and the duration of extraction

1 g of plant material was extracted with 50 ml of each solvent, on boiling water-bath under reflux. After cooling, extracts were filtered in 50 ml volumetric flasks and made up with appropriate solvent. 10 ml of each extract was submitted to hydrolysis with 10 % chloride acid and after that whole flavone contents were re-extracted with ethyl acetate. 2 ml of washed ethyl acetate extract were diluted in 25 ml volumetric flask with methanol to volume. The last solution was used for absorbance measurements at 336 nm.

Procedure

0.5-1.0 g of milled plant material was transferred in an erlenmeyer flask and heated with 50 ml mixture ethanol:water (70:30 v/v) on boiling water-bath, under reflux, for 2 hours. After cooling, solution was filtered in 50 ml volumetric flask and made up with ethanol. 10 ml were submitted to hydrolysis with 25 % chloride acid on water-bath, under reflux, for 30 min. After cooling, mixture was mixed with 20 ml of water and than extracted with 15 ml of ethyl acetate, three times. Ethyl acetate extract was washed with 50 ml of water three times and filtered in 50 ml volumetric flask and made up with ethyl acetate. 2 ml of the last were transferred in 25 ml volumetric flask, added with 0.5 ml of 0.5 mol/L solution of NaOH and diluted to volume with methanol. Other 2 ml were diluted in 25 ml volumetric flask to volume with methanol. After 20 min (but not more than 40 min) the absorbance of the solution that contained NaOH was measured at 390 nm against the solution without addition of NaOH that was used as blank.

Calibration curve for determination of flavonoids (apigenin)

Stock solution (100 μg/ml): 10 mg of apigenin were dissolved in methanol in 100 ml volumetric flask and made up with methanol.

Primary stock solution (10 μg/ml): 10 ml of stock solution were diluted with methanol in 100 ml volumetric flask and made up with methanol. In 10 ml volumetric flasks, 1-10 ml of the solution were diluted with methanol, added with 0.5 ml 0.5 mol/L solution of NaOH and made up with methanol (1-10 μg/ml apigenin). In other 10 ml volumetric flasks the same solutions were prepared without addition of NaOH that were used as blanks. After 20 min absorbance was measured at 390 nm.

Results and discussions

A methanol spectra of plant flavonoids (Thymus tosevii ssp. tosevii) is shown at Figure 1a.

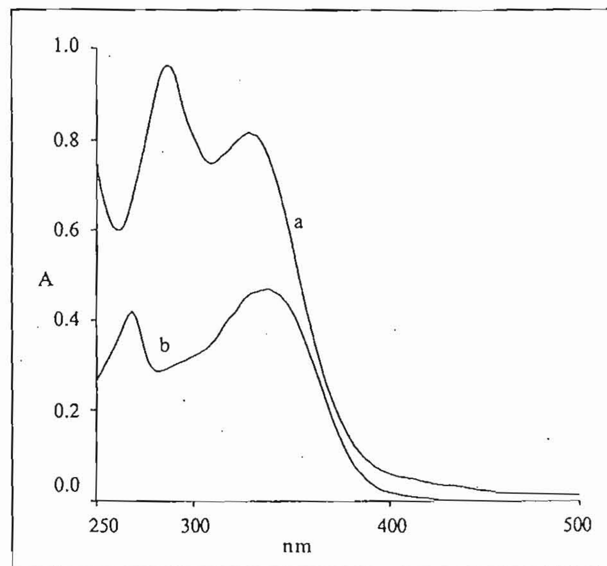

Fig. 1: UV/VIS spectra of flavonoids from plant methanol extract (a) and apigenin in methanol (b)

The absorption spectra of plant flavonoids showed two major absorption bands at 286 nm and 330 nm that could be recognized as Band I and Band II [25]. The position of Band I point at possibility of a presence of flavone components in certain plant methanol extract. Comparing this spectra with absorption spectra of apigenin (Fig. 1b.) a resemblance was found in the area of Band I, because in the apigenin absorption spectra Band I occurred at 336 nm Until now, data concerning isolation and identification of flavonoid components in the taxa of genera Thymus mostly referred to the presence of mainly flavone components, very often highly oxygenated and methylated [15-24]. Few flavones has been established as characteristic for the most of Thymus taxa, as apigenin, luteolin and 6-hydroxyluteolin [15], than xanthomicrol, cirsilineol and cirsimaritin [15] as well as naringenin, eryodictyol and methylcirsilineol [24]. Because, occurrence of apigenin is very common in various Thymus taxa and absorption spectra of plant flavonoids was found to be very similar to absorption spectra of apigenin, especially in the area of Band I, apigenin was chosen as authentic marker of flavonoids for calculation their contents in plant material.

1. Determination of an appropriate extraction agent and establishing the duration of extraction

The extraction agent was chosen by preparation of several different extracts from certain plant using different solvents (methanol, ethanol or mixtures of ethanol and methanol with water in various volume ratio). The duration of extraction was changed from 30 to 180 min.

From the obtained results it could be concluded that when the mixture of ethanol:water (70:30 v/v), as well as the mixture of methanol:water (70:30 v/v) were used for extraction, the highest absorbance has been registered in the final solutions. In our further examination the mixture of ethanol:water (70:30 v/v) was chosen as the most appropriate extraction agent for whole flavonoid content from examined plant material. It takes 2 hours for extraction.

2. Determination of an appropriate hydrolysis agent and establishing the duration of hydrolysis

In the previously carried out phase, 1 0 % chloride acid was used for hydrolysis of flavonoid glycosides. Hydrolysis with this acid is very common for various plant components [26]. But, in our examination, hydrolysis with 10 % chloride acid implicated 2 hours which is very long period for this phase of methodological procedure. That point at need for establishing more appropriate hydrolysis agent which would provide with shorter duration. For that purpose, 5 % sulphate acid, 5 % chloride acid and 25 % chloride acid were also used for hydrolysis. The duration of hydrolysis was changed from 15-150 min.

The highest absorbance value, obtained from the methanol plant extract as well as the highest content of „flavonoids" in the plant sample, was provided by use of 25 % chloride acid for hydrolysis when it implicated 30 min. Similar results were obtained by use of 10 % chloride acid and 5% sulphate acid but hydrolysis in those cases took 2 hours. In our further examination 25 % chloride acid was used as the most appropriate hydrolysis agent and 30 min duration of hydrolysis was established as the most available.

3. Determination of an appropriate extraction agent for the whole flavone content after hydrolysis

The next phase that need to be solved was determination of an appropriate agent for extraction of whole flavonoid content after hydrolysis that means free flavone and the aglycones obtained after hydrolysis of glycosides forms. The same procedure was carried out as was mentioned above. Only the extraction agent for extraction of flavonoids after hydrolysis varied from ethyl acetate, ether, chloroform, benzene and hexane. The results showed that use of ethyl acetate for extraction of whole flavonoids was the most appropriate because it provides the highest content value of total „flavonoids" in certain plant sample. More than this, ethyl acetate could be easily diluted with methanol which made it much more available than other solvents that couldn't be mixed with methanol.

4. Establishing a reagent for bathochromic shift in absorption spectra of flavonoids (apigenin)

Spectrophotometric determination of total flavonoids in plants mostly includes addition of a complex reagent that provokes bathochromic shift in absorption spectra of flavonoids [1, 2-10]. Because most of data point at an use of $AlCl_3$ as complex reagent [1, 9-11] it was applied in our examination. The procedure given by Chirst and Muler [9] is based on determination of flavonoids by absorbance measurements at the wavelength of the maximum of absorption in a compensation spectra. This spectra was made by recording the spectra of methanol solution of flavonoids in presence of $AlCl_3$ against the same solution that didn't contain $AlCl_3$, and was used as blank. Thus, in the case of quercetin the maximum absorption of compensation spectra appears at 425 nm. By recording the compensation spectra, measured absorbance mostly due to the absorption of flavonoid complex with $AlCl_3$, but even then, certain influence on absorbance from the other components that absorb at 425 nm was presented.

Methanol absorption spectra of plant flavonoids in presence of $AlCl_3$ and their compensation spectra are presented at Figure 2. Maximum absorption in compensation spectra of plant flavonoids occurred at 390 nm, but the value of absorbance is very low.

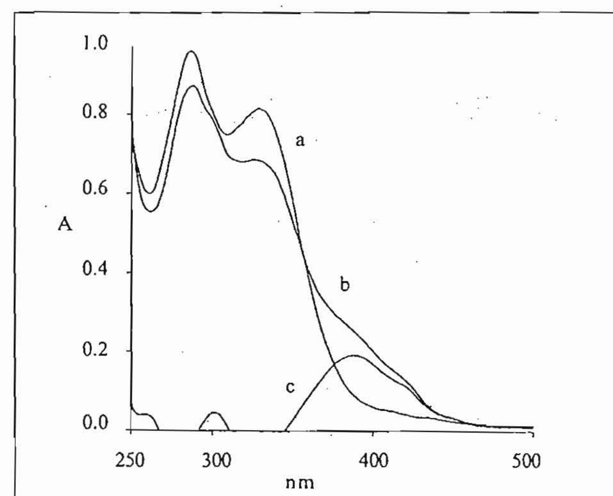

Fig. 2: UV/VIS spectra of flavonoids from plant methanol extract (a), UV/VIS spectra of the same flavonoids with addition of $AlCl_3$ (b) and „compensation spectra" of the flavonoids with $AlCl_3$ (c)

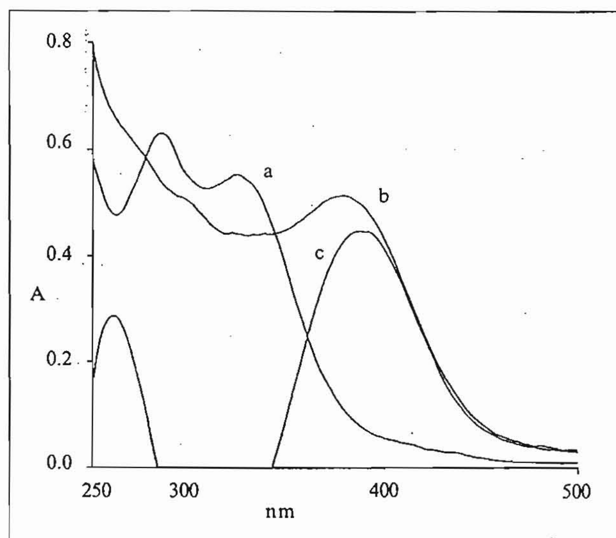

Fig. 3: UV/VIS spectra of flavonoids from plant methanol extract (a), UV/VIS spectra of the same flavonoids with addition of NaOH (b) and „compensation spectra" of the flavonoids with NaOH (c)

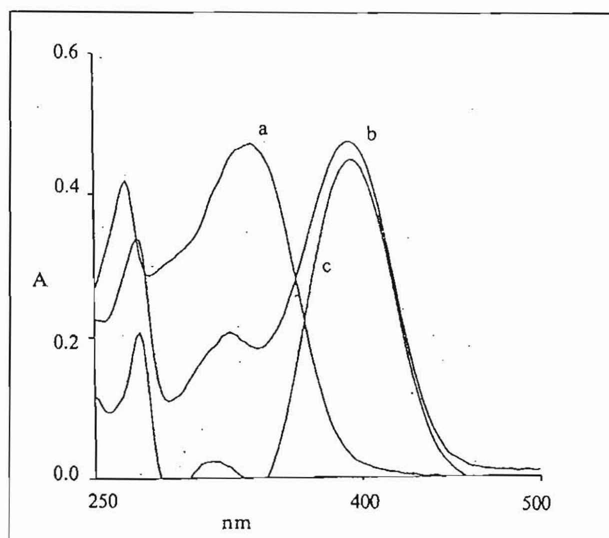

Fig. 4: UV/VIS spectra of apigenin in methanol (a), UV/VIS spectra of apigenin with addition of NaOH (b) and „compensation spectra" of apigenin with NaOH (c)

It is well known that beside Al^{3+} ions, few other could be used for making complexes with flavonoids, as was already mentioned above. In our examination it was decided to change the type of reaction of flavonoids and for that purpose 0.5 mol/L water solution of NaOH was used [12]. The decision was based on the following: From the data concerning to identification of different flavonoids in various Thymus taxa (apigenin, luteolin, 6-hydroxyluteolin, genkwanin, chryseriol, cirsilineol, cirsimaritin, thymonin, thymusin, xanthomicrol, siderithoflavon, etc.) [13-24] it appears that each of them exhibit 4'-OH group free. It is known that if the flavonoids have 4'-OH group free, presence of sodium hydroxide provokes bathochromic shift in their absorption spectra, exactly Band I is shifted [12, 25].

The absorption spectra of plant flavonoids in presence of NaOH and compensation spectra with NaOH are shown at Figure 3. The maximum absorption in the compensation spectra occurred at 390 nm, the same wavelength that was exhibited in the case when $ALCL_3$, was used as shifting reagent. But, when the solution of NaOH was used, the value of absorbance was much more higher.

The methanol absorption spectra of apigenin in presence of NaOH as well as the compensation spectra of apigenin with NaOH are shown at Figure 4. The maximum absorbance in the compensation spectra of apigenin in presence of NaOH occurred at 390 nm. The molar absorption coefficient of apigenin with NaOH was ε_k=24600 $mol^{-1}dm^3cm^{-1}$. Calibration curve of apigenin in presence of NaOH showed linearity in concentration range 1.0-10.0 μg/ml. The regression line estimated by linear-squares regression analysis was represented by the equation A=0.015+0.0752c. The correlation coefficient was 0.9996.

4.a. Influence of coffeic acid on the determination of apigenin

Spectrophotometric methods for determination of total flavonoids by involving addition of some reagents that provoked bathochromic shift in absorption spectra of flavonoids, provided separation of flavonoids from other components that absorbed in UV spectral area. However, it is desirable to add more selective reagent that react only with flavonoids. It is well known that NaOH is not selective enough and beside flavonoids reacts with phenol acids, if they are also presented in the same solution. Because of that, the influence of coffeic acid presented in the solution of apigenin on the determination of the apigenin was observed. First of all, absorption spectra of coffeic acid in presence of NaOH was recorded as well as the spectra of a mixture of apigenin with coffeic acid in presence of NaOH. This spectra are shown at Figure 5. As could be seen from the figure, presence of coffeic acid didn't change the form of apigenin spectra. To check the influence on the absorbance that coffeic acid probably has at 390 nm, solution of apigenin with known concentration was prepared with known additions of coffeic acid. The solution of NaOH was added and after 20 min the absorbance of the mixtures was measured at 390 nm. Similar to this mixtures, other were prepared without addition of NaOH that were used as blanks. The results of this examination are presented in Table 1. Similar to this examination other was carried out, too, but with $AlCl_3$ as shifting reagent. The results are also presented in Table 1.

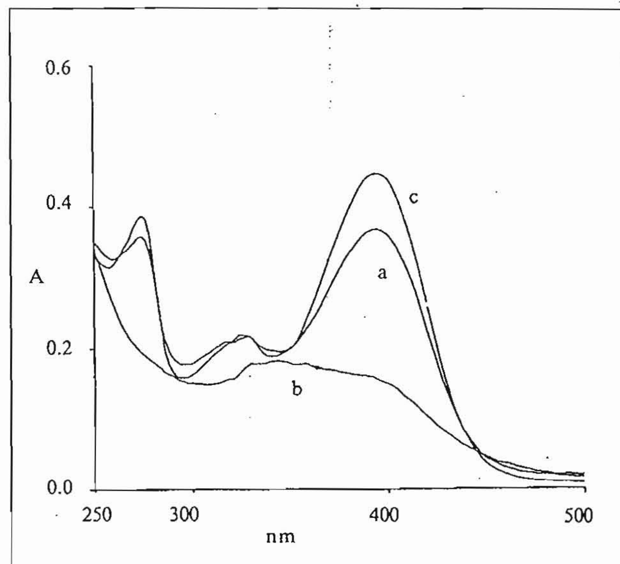

Fig. 5: UV/VIS spectra of apigenin with addition of NaOH (a), UV/VIS spectra of coffeic acid with NaOH (b) and UV/VIS spectra of apigenin: coffeic acid mixture (1:1) with NaOH (c)

Table 1. **Determination of apigenin in presence of coffeic acid**

Added coffeic acid (μg/ml)	Determined apigenin (μg/ml)		Error in determined apigenin (%)	
	NaOH	$AlCl_3$	NaOH	$AlCl_3$
-	0.90	0.90	0	0
0.5	0.90	0.87	0	-3.3
1.0	0.92	0.83	+2.2	-7.8
1.5	0.93	0.77	+3.3	-14.4
2.0	0.95	0.72	+5.5	-20.0

From the results given in the Table 1, it appears that presence of coffeic acid had some influence on absorption when the concentration of coffeic acid was once or twice more than concentration of apigenin in the same solution. Presence of coffeic acid in those cases gave an increase of concentration of apigenin in range 2.2 % to 5.5 %. In the case when $AlCl_3$, was used the obtained results for concentration of apigenin were lower with a decrease of 3.3 % to 20.0 %. In this case, it should be pointed out that the value of absorbance was very unstable and absorbance measurements were hard to make.

4.b. Determination of stability of apigenin solution in presence of NaOH

For determination of stability of the product of reaction between plant flavonoids (or apigenin) and NaOH, absorbance of the methanol solution of flavonoids (apigenin) was measured 20, 30, 40, 60, 90 and 120 min after addition of NaOH. It was established that the absorbance of the examined flavonoids (apigenin) solution in the presence of NaOH hasn't changed in the first 40 min. After that period of time absorbance started to decrease and that provoked error in determined concentration of flavonoids (apigenin) in range 2.5 % to 5.0 %.

5. Checking the suggested procedure

The suggested procedure for determination of total flavonoids in the Thymus taxa was checked by method of standard additions. Namely, in the samples wherein the content of flavonoids was previously determined, quite known quantity of apigenin was added and after that, the content of whole flavonoids (naturally presented and added) was determined by suggested procedure. The results of this examination are presented in Table 2. The recovery value was satisfactory, ranged from 101.4-103.3 %.

Table 2. **Determination of total flavones in *T. tosevii ssp. tosevii* by method of standard additions (apigenin)**

Added apigenin μg/ml	Calculated apigenin μg/ml	Determined apigenin μg/ml	R (%)
-	-	5.05	-
0.50	5.55	5.63	101.4
1.00	6.05	6.23	103.0
1.50	6.65	6.88	103.3

Similar to this examination, other one was carried out whereby the known volume of the plant extract was added to the primary taken volume and then the determination of flavonoids was carried out by the procedure. The results of this examination, given in Table 3, showed satisfactory value for recovery ranged 99.2 – 100.1 %.

Table 3. **Determination of total flavones in *Thymus tosevii ssp. tosevii* by suggested procedure with additions of certain quantities of plant extrat**

Added quantity of plant extract (ml)	Added quantity of flavones μg/ml	Expected concentration μg/ml	Determined concentratio μg/ml	R (%)
-	-	-	5.86	-
5	5.86	11.72	11.62	99.2
10	11.72	17.58	17.60	100.1
15	17.58	24.44	24.32	99.5

6. Determination of total flavonoids in samples of Thymus taxa

Twenty-three different samples that belonged to eleven different taxa of the genera Thymus were submitted to determination of total flavonoid contents. The results given in Table 4 showed that the content of total flavonoids was in range 0.53-2.59 % and relative standard deviation - RSD was 1.43-8.65 %. Only one sample (Thy-

mus ciliatopubescens) cootained lower amount of flavonoids (0.53 % with RSD of 11.32 %). The other taxa of the genera Thymus that occur in flora of Republic of Macedonia represent an interesting plant source of flavonoid components.

Table 4. Results from determination of total flavones in the taxa of genera *Thymus* L., calculated as apigenin

Plant material	w/ (%)	SD	RSD (%)
Thymus tosevii Velen. *ssp. tosevii var. tosevii*			
– Raiko Žinzifov, Veles, 1993	1.09	0.05	4.59
– Ljubanci, Skopje, 1993	1.18	0.05	4.24
– Nicolić, Dojran, 1994	1.42	0.03	2.10
– Vitačevo, Kavadarci, 1994	1.66	0.07	4.22
– Majdan, Alšar, 1994	1.08	0.06	5.46
– Laki, Berovo, 1994	1.82	0.10	5.49
Thymus tosevii Velen. *ssp. tosevii var. degenii* (H.Br.) Ronn.			
– Karadžica mountain, 1994	2.59	0.12	4.63
– Vrben, Mavrovo, 1994	2.29	0.16	6.99
Thymus tosevii Velen. *ssp. tosevii var. longifrons* Ronn.			
– Karadžica mountain, 1994	1.79	0.07	3.91
Thymus tosevii Velen. *ssp. substriatus* (Borb.) Matevski			
– Nicolić, Dojran, 1994	1.64	0.12	7.32
– Vitačevo, Kavadarci, 1994	1.95	0.12	6.15
Thymus longidens Velen. *var. lanicaulis* Ronn.			
– Sonje, Skopje, 1993	1.43	0.08	5.59
– Sonje, Skopje, 1994	1.62	0.04	2.47
– Banjani, Skopje, 1994	1.43	0.04	2.80
Thymus longidens Velen. *var. dassareticus* Ronn.			
– Karadžica mountain, 1994	0.96	0.04	4.17
Thymus alsarensis Ronn.			
– Majdan, Alšar, 1994	2.04	0.09	4.41
Thymus macedonicus (Degen et Urumov) Ronn.			
– Laki, Berovo, 1994	1.40	0.02	1.43
Thymus moesiacus Velen.			
– Popova Šapka, Šar Planina, 1993	2.15	0.06	2.79
– Popova Šapka, Šar Planina, 1994	1.33	0.05	3.76
– Bistra mountain, 1994	1.56	0.06	3.85
Thymus ciliatopubescens			
– Sonje, Skopje, 1994	0.53	0.06	11.3
Thymus albanus H. Braun			
– Popova Šapka, Šar Planina, 1993	1.04	0.09	8.65

References

1. Stanić, G., B. Katušin-Ražem, J. Petričić. *Farm. Glas.*, 41, 1988, 179.
2. Constantinesco, D. G., R. Oteleanu. *Acta Pol. Pharm.*, 14, 1957, 27.
3. Kucharsky, J., *Česk. Farm.*, 6, 1957, 91.
4. Bross, T., U. Bilinska. *Acta Pol. Pharm.*, 15, 1958, 394.
5. Hogedorn, P., R. Neu,. *Arch. Pharm.*, 284, 1953, 486.
6. Horhammer, L., R. Hansel. *Arch Pharm.*, 282, 1951, 276.
7. Radović, Z., D. Malešev. *Pharmazie*, 38, 1984, 870.
8. Malešev, D., Z. Radović. *Pharmazie*, 42, 1987, 57.
9. Christ, B., K. H. Muller. *Arch. Pharm.*, 293, 1960, 66.
10. DAB 10.
11. Wagner, H., G. Tittel, S. Bladt. *Deut. Apoth. Ztg.*, 123, 1983, 515.
12. Kemertelidze, E. P., V. P. Georgievskii. Fizikohemičeski metodi analiza nekotorih biologičeski aktivnih višesv rastitelnogo proishoždenia, Mecniereba, Tbilisi, 1976, p. 125.
13. Van den Broucke, C. O., R. A. Dommise, E. L. Esmans, J. A. Lemli. *Phytochem.*, 21, 1982, 2581.

14. Voirin, B., M. R. Viricel, J.Favre-Bonvin, C. O. Van den Broucke, J. Lemli. *Plant. Med.*, 5, 1985, 523.
15. Marhuenda, E., C. Alkoron de la Lastra, M. D. Garcia, A. Cert. *Ann. Pharm. Fran.*, 45, 1987, 467.
16. Washington, J. S., U. K. Saxena. *J. Inst. Chemist. (India)*, 57, 1985, 153.
17. Tomas, F., L. Hernandez, F. A. T. Berberan, F. Ferreres. *Z. Naturforsvh.*, 40, 1985, 583.
18. Ferreres, F., F. A. T. Barberan, F. Tomas, L Hernandez. *Plan. Med. Et Phytoth.*, 19, 1985, 89.
19. Barberan, F. A. T., L. Hernandez, F. Ferreres, F. Tomas. *Plant. Med.*, 5, 1985, 452.
20. Hernandez, L. M., F. A. T. Barberan, F. T. Lorente. *Biochem. Syst. Ecolog.*, 15, 1987, 61.
21. Hernandez, L., F. A. T. Barberan, F. T. Lorente. *Biochem. Syst. Ecolog.*, 16, 1988, 43.
22. Adzet, T., F. Martinez. *Bioch. Syst. Ecolog.*, 9, 1981, 293.
23. Barberan, F. A. T., E. Wollenweber. *Plant. Syst. Evol.*, 173, 1990, 109.
24. Adzet, T., R. Vila, S. Conigureal. *J. Ethnopharm.*, 24, 1988, 147.
25. Mabry, T. J., K. R. Markham, M. B. Thomas. The sistematic identidication of flavonoids. New York, Haidelberg, Berlin, Springer-Verlag, 1970, p. 32.
26. Harborne, J. B. Phytochemical Methods. London, Champan and Hall, 1973, p. 33.

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ТЕХНОЛОГИЧНИ И БИОФАРМАЦЕВТИЧНИ ПРОУЧВАНИЯ ПРИ СЪЗДАВАНЕ НА ЛЕКАРСТВЕНИ ФОРМИ С ИЗОПРОПИЛАНТИПИРИН (ПРОПИФЕНАЗОН). III. БИОФАРМАЦЕВТИЧНИ ИЗСЛЕДВАНИЯ ПРИ СЪЗДАВАНЕ НА СУСПЕНЗИЯ С ПРОПИФЕНАЗОН

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TECHNOLOGICAL AND BIOPHARMACEUTICAL INVESTIGATIONS ISOPROPILANTIPYRIN (PROPIFENAZON) FORMULATIONS. III. BIOPHARMACEUTICAL INVESTIGATIONS OF PROPIFENAZON SUSPENSION

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РЕЗЮМЕ: Целта на настоящата работа е създаване на суспензия с пропифеназон, получена от гранули. Проведени са изследвания, отнасящи се, от една страна, до гранулите, а, от друга – на суспензията. Изследвано е влиянието на редица фактори и помощни вещества (Avicel, нишесте, манитол, сорбитол, ПАВ) за получаване на гранули, отговарящи на изискванията (разпадаемост, механична якост, реологични свойства). Изследвани са седиментационният процес и реологичните свойства на модели суспензии. Проучен е процесът на in vitro преминаване на пропифеназон през липидна мембрана и имитираща стомашна стена (по Stricker).

Ключови думи: пропифеназон, гранули, суспензия, in vitro освобождаване

SUMMARY: The aim of this paper is a suspension whit propifenazone made from granules. There were made investigations concerning on one side the granules, and on the other – the suspension. It was investigated the influence of several factors and exipients (Avicel, watersoluble starch-manitol, sorbitol, sulfactants) for the preparation of granules, fulfilling the requirements (desintegrations, hardness, rheological properties). The sedimention and rheological properties of suspension models, were investigated. It was studied the process of in vitro penetration of propifenazone through a lipid stomach membrane – Stricker.

Key Words: Propifenazone, Granules, Suspension, In vitro, Penetration

Целта на настоящото изследване е създаване на суспензия с пропифеназон, получена от гранули, предназначени за деца.

Пропифеназонът притежава ограничена разтворимост във вода. Това изисква провеждането на обстойни изследвания за влиянието на редица биофармацевтични фактори върху неговата биологична наличност.

Разработваната от нас форма изисква, от една страна, изследвания, свързани с получава-