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RESEARCH TO IMPROVE THE THERAPEUTIC PERFORMANCE OF A NUTRITIONAL SUPPLEMENT WITH HYPOGLYCEMIC ACTION

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Abstract

The following study presents a series of practical aspects regarding the development of tablet formulations containing hypoglycemic plant extracts. The selected preparation methods were wet granulation and direct direct compression, studied comparatively. Plant materials such as Agrimoniae herba, Lythri salicariae herba, Myrtilii folium, Mori folium, Phaseoli were used. The excipients were as following: microcrystalline cellulose, polyvinylpyrrolidone, sodium glycolate starch and Ludipress. Four formulations were developed, differing by excipient content, so as to permit selection according to compendial requirements. The tablets were qualitatively evaluated regarding organoleptic assessment, uniformity of mass and content, disaggregation time, friability determination. The fourth formulation was selected, containing the excipient Ludipress serving as diluent, binding agent, and disintegrant also. The prepared formulation represents a potential dietary supplement as part of the adjuvant therapy of diabetes.

Key words: hypoglycemiant supplement, natural extracts, direct compression

INTRODUCTION

The specialty literature mentions many herbs that can be used in the treatment and prophylaxis of diabetes and complications of diabetes (Lu T. et al, 2012). The preparation of this work is based on practical considerations in pursuing tablets containing plant extracts with hypoglycemic action, using the method of preparing the wet granulation and direct compression, which were studied in comparison (Jaiswal D. et al, 2009; Istudor Viorica, 2001).

The studies herbs were: Agrimoniae herba, Lythri salicariae herba, Myrtilii folium – containing flavonoids and tanins, Mori folium containing flavonoids, Phaseoli fructus – for its isoflavonids, soluble silicates and chromium salts. From these herbs were obtained selective dried extracts (Bruneton J.,2005; Velescu B.Şt, 2012).

MATERIAL AND METHOD

Formulating tablets

The first three formulas contain plant extracts and the following inactive ingredients: Avicel Ph 102 (microcrystalline cellulose), polyvinylpyrrolidone, Primojel (Sodium starch glycolate), talcum and magnesium stearate.

Qualitative and quantitative composition of the tablets is shown in Table l.

Tabel 1

The composition of the medicinal product

Components	**Formula 1 Quantity/tablet (g)**	**Formula 2 Quantity/tablet (g)**	**Formula 3 Quantity/tablet (g)**	**Formula 4 Quantity/tablet (g)**	**Its role in the formulation**
Agrimoniae Herba Extract	0,1	0,1	0,07	0,07	Active sustance
Myrtilli Folium Extract	0,1	-	0,065	0,065	Active substance
Salicarie Herba Extract	-	0,1	0,065	0,065	Active substance
Mori Folium Extract	0,2	0,2	0,2	0,2	Active substace
Phaseoli Fructus Sine Siminubus Extract	0,2	0,2	0,2	0,2	Active substance
Avicel PH 102	0,05	0,05	0,05	-	Thinner
Polyvinylpyrrolidone	0,004	0,004	0,004	-	Binder
Primojel(sodium starch glycolate)	0,025	0,025	0,025	-	Disintegrater
Talcum	0,004	0,004	0,004	0,004	Lubricate
Magnesium stearate	0,004	0,004	0,004	0,004	Lubricate
Ludipress	-	-	-	0,15	Thinner, binder, disintagrater

Characterization of plant extracts

The studied plants were: Agrimoniae herba, Lythri salicariae herba, Myrtlii folium – for their content in flavonoids and tanins, Morii folium for its content in flavonoids, Phaseoli fructus – for its isoflavonoids, soluble silicates and chromium salts (Table 2). From these herbs were obtained selective dried extracts (Dobjanschi L., 2005; Mihele D., 2006).

The technology used to obtain the extracts (choice of solvents, the number of extractions, the ratio product / solvent and the extraction method) it was determined according to FR X (based on the amount of extractables

substances and active principles)(Farmacopeea Română, ediţia a-X-a, 2008).

The quality of the results was verified by: chemical examination (specific reactions for identification and dosage), and determinating the toxicity and hypoglycaemic action.

Table 2

Quality of plant extracts

No.	Extract	Humidity (%)	Flavonoids (%) (expressed as rutoside)	Poliphenolic compounds (%) expressed as caffeic acid)
1	Salicariae Herba	10,44 - 11,99	0,14 - 0,58	1,03 - 1,73
2	Phaseoli fructus	6,05 - 6,56	0,36 - 0,55	0,16 - 2,02
3	Morii folium	9,33 - 13,90	0,76 - 0,96	1,37 - 3,61
4	Myrtilli folium	7.46 - 7,82	0,96 - 1,22	32,68 - 41,62
5	Agrimoniae Herba	8,03 - 11,81	0,69 - 0,81	23,38 - 27,40

Preparation of tablets from plant extracts

For tablet formulations F1, F2 and F3 it was applied the method of wet granulation and for preparing the tablets based on plant extracts, it was applied the F4 formula, which is the direct compression, respecting all parameters of the process. The fourth formulation containing Ludipress – new excipient, modern, obtained by co-processing, in this case the tablets were obtained by direct compression method (Vicaș L., 2011; Popivici I., Lupuleasa D., 2013; European Pharmacopeea 8.1, 2016).

RESULTS AND DISCUSSION

European Pharmacopoeia specified a number of conditions on uncoated tablets. In addition to identification, the determination of chemical purity and content of the active substance. There are a number of standards that are designed to ensure that the patient receives a stable product containing the active substance in the required amount a formulation that allows the substance to manifest throughout the pharmacological activity. These standards are: content of active substance; mass uniformity, content uniformity; disintegration time; Dissolution rate (Farmacopeea Română, ediţia a-X-a, 2008). Fiabilitatea and mechanical strength are mentioned in the pharmacopoeia but they are not equally important (Suplimentul Farmacopeiei Române, 2004).

A. Organoleptic control

Appearance: uncoated tablets, the payment form, with margins intact, smooth surface, unprinted.

The height of the tablets: up to 4 mm

Color: brown – gray

Taste: Easy bitter

Average weight: 690 mg / tablet (F1 - F3), 750mg / cpr. (F4).

B. Determination of mechanical strength

The tablets obtained must be tough enough to withstand the shock elimination from the compressed drive, packing and handling, but can be broken if the patient will receive one half or one quarter of a tablet. For practical determination of the hardness of the tablets was used Vankel VK device 200 (Tablet Hardness Tester).

The machine uses a measuring system for measuring hardness with progressive tension. It is controlled by a microprocessor constituted inside. Clamping device is connected to the strain gauge transducer. They were tested a total of six tablets. The results obtained are shown in Table 3.

Table 3

Determination of the mechanical strength of tablets

No.	Mechanical strength (kp)			
	Formula 1	Formula 2	Formula 3	Formula 4
1	17	18	17	13
2	18	19	17	15
3	18	17	16	14
4	15	16	18	14
5	17	18	17	16
6	17	17	16	15
Average	17	17.5	16.83	14.5

The results are within the acceptable limits. In the first three formulations, the PVP was used as binder, they are very close to the values obtained. The tablets obtained by direct compression have a lower resistance.

C. Determination of friability tablets

Although tablets fulfill the requirement of strength, it is possible that they have a tendency to crumble, which is expressed by friability. The device used to determine the friability consists of two drums rotating

Plexiglas with a diameter of 30 cm and a thickness of 4 cm, the rolling and falling of the tablets is performed by a curved upright The drums are rotated by a motor 25 synchronously with the revolutions per minute, using a spatula inside the drum is recurved. Less resistant tablets break or wear out the edge.

We used 10 tablets and were subjected to 100 revolutions for 4 minutes. Weight loss is calculated using the formula:

$$\text{Friability} = \frac{M_1 - M_2}{M_1} \times 100$$

where:

M_1 – tablets initial mass in g

M_2- mass of dedusted tablets after the test in g

It admits a loss under 1%.

Table 4

Determination of friability tablets

No.	**Friability (loss)%**			
	Formula 1	**Formula 2**	**Formula 3**	**Formula 4**
1	0,5	0,5	0,4	0,8
2	0.4	0.7	0.4	0,7
3	0.5	0.6	0.5	0,8
4	0.5	0.5	0.4	0,8
5	0.6	0.4	0.4	0,9
6	0.5	0.5	0.6	0,7
7	0.6	0.5	0.5	0,7
8	0.5	0.5	0.4	0,7
9	0.5	0.8	0.4	0,8
10	0.4	0.5	0.5	0.9
Average	0,5	0,55	0,45	0.78

The results obtained from the test of reliability falls within the maximum limit of 1%.

D. Determination of mass uniformity

According to FR X we weigh 20 tablets and determine the average weight. The same tablets weighed individually Compared to the average mass calculated individual weights have certain percentage deviation entered in FR X.

Table 5

Determination of mass uniformity

No.	Weight (mg)			
	Formula 1	**Formula 2**	**Formula 3**	**Formula 4**
1.	687	690	680	750
2.	685	690	679	750
3.	686	689	678	750
4.	684	693	683	749
5.	685	691	677	748
6.	683	690	680	750
7.	685	687	680	751
8.	684	688	681	752
9.	686	690	680	753
10.	685	692	682	750
11.	685	691	682	747
12.	685	692	679	748
13.	684	688	678	749
14.	686	687	680	748
15.	685	689	680	750
16.	684	691	680	750
17.	687	693	683	752
18.	686	690	680	752
19.	683	689	677	751
20.	685	690	681	750

E. Determination of disintegration time

Disintegration time according to FR X is determined using a test equipment Electrolab TDT-08L Dissolution Tester (USP)

The number of movements is 23-24 / min and amplitude is 50-60 mm.

The device performs movements in the cylindrical vessel into which the liquid medium is introduced. Thermostat bath into which the cylindrical vessel must ensure that the temperature of the liquid medium at 37 ° C (Table 6).

Table 6

Determination of disintegration time

No.	Disaggregation time needed (min)			
	Formula 1	**Formula 2**	**Formula 3**	**Formula 4**
1	8,5	6,9	7,5	5.6
2	9,2	7,2	7.0	5,8
3	7,8	6,7	6.4	4,9
4	8,6	7,0	6,9	4,6
5	9,1	6,8	7,2	5,0
6	9,0	7,1	6,8	5,7

The results obtained fall within the maximum allowed by FR X 15 minutes.

CONCLUSIONS

The best results in the treatment of diabetes means associating herbal extracts that are obtained from selective plants which the literature indicates that have the hypoglycaemic effect. Plant products ordered herein, which were obtained dried extracts were selected: Agrimoniae herba, Lythri salicariae herba, Myrtilii folium for their content in flavonoids and tanins (catehice and galenice) Mori folium for its content in flavonoids and moraline, Phaseoli fructus- for its isoflavone, soluble silicates and chromium salts.

They were developed and made practical four tablet formulations: the first formula (F1) contains dry extract obtained from Agrimoniae Herba, extract from Myrtilli Folium, extract from Mori folium and extract from Phaseoli Fructus sine Siminibus alongside these extracts are added the following ingredients: Avicel PH 102, polyvinylpyrrolidonePrimojel, talcum and magnesium stearate; formula two (F2) contains extract from Agrimoniae Herba, extract from Salicarie Herba, extract from Mori Folium, extract from Phaseoli Fructus sine Siminibus alongside these extracts are added and excipients listed in the first formula.

The third formula (F3) contains all five plant extracts and the same excipients used and the previous formulas. The method of preparation in the case of formulations F1 - F3 is compression after wet granulation. The last formulation (F4) comprises, in addition to the plant extracts, Ludipress disintegrating binder excipient diluent modern has many advantages to classical excipients and direct compression process enables application.

Features of the experimental formulations have allowed the smooth implementation of the technological process standard to a laboratory scale plant extracts in order to obtain tablets with hypoglycaemic activity.

Preliminary research results on the formulation and obtaining on a laboratory scale experiments tablets in conjunction with preclinical and clinical results can be the basis for obtaining new pharmaceutical product with hypoglycaemic.

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