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EXPERIMENTAL PAPER

Selected excipients and surfactants in oral solid dosage form with extract of *Phaseoli pericarpium* (*Phaseolus vulgaris* L.)

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Summary

Introduction: The common bean (*Phaseolus vulgaris* L.) is an annual plant grown in many countries all over the world including its different varieties in Poland. Herbal raw material are elongated pods – pericarp. *Phaseoli pericarpium* decreases the glucose blood level. *Phaseoli pericarpium* extracts manifest duretic properties, can be used in the treatment of edema, kidney diseases with decreased urinary excretion, nephrolithiasis. **Objectives:** To investigate the usefullness of selected excipients as carriers of dry extract from *Phaseolus vulgaris* pericarp. **Methods:** The method of direct tableting was used. In the further stage, the obtained tablets were subjected to appropriate tests. The first stage of the study evaluates Prosolv SMCC 50, PROSOLV EASYtab, EMDEX, Carmellose calcium and PRUV. These were used to manufacture 4 batches of tablets. In the second stage, an oral solid dosage was manufactured on the basis of the formulation composition of batch 1 tablets (*Phaseoli pericarpium* extract, Prosolv SMCC 50, PRUV). Then, different surfactants (cholesterol oxyethylate $n_{TE} = 30$, cholesterol oxyethylate $n_{TE} = 40$, Rofam $n_{TE} = 50$), were successively added to this formulation, to obtain 3 batches of tablets. All 7 batches were manufactured in the Erweka tableting machine. Then, they were subjected to morphological tests and physicochemical evaluation. The release of active substances to 3 selected acceptor fluids (water, artificial gastric juice, artificial intestinal juice) was measured in accordance with the requirements of the general and specific monographs in European Pharmacopoeia 7. **Results:** The manufactured tablets had a smooth uniform surface with no stains, spalls or mechanical damage and yellow color originating from the extract. The obtained tablets, with surfactants in their com-

position, demonstrated pharmaceutical availability slightly higher than batch 1 tablets without surfactants. **Conclusions:** Excipients applied in appropriate proportions appear to be useful in the manufacturing of uncoated tablets containing extract of *Phaseoli pericarpium*.

Key words: *Phaseolus vulgaris, direct tableting, surfactants, excipients*

INTRODUCTION

Phaseolus is a genus of the family *Fabaceae* including about 200 species of annual and perennial plants, vines and subshrubs with large leaves and white, yellow or red flowers [1]. The common bean (*Phaseolus vulgaris* L.) belongs to this family. It is an annual plant originating from South America. It is cultivated in many countries, including Poland, for food, dry seeds and immature pods. It exhibits a wide variety of seed coat patterns and colors [2, 3].

The pharmacopoeic material described in the Polish Pharmacopoeia VI [4] is the dried pericarp (bean pod, *Phaseoli pericarpium*) derived only from white-flowered cultivars of *Phaseolus vulgaris*. The pericarps are curled and slightly thin, up to 20 cm long and up to 2 cm wide. One end has a short beak-like point, while a 1 cm stalk is often attached to the other. The outside surface is pale yellow or dark brown yellow, the inside is covered with a whitish, shiny membrane. In the areas where seeds are present, the pericarp is concave inside and convex outside [4].

The main pharmacologically active compounds of *Phaseoli pericarpium* are: choline, amino acids (arginine, asparagine, leucine, lysine), pipecolic acid, trigonelline, allantoin, phenolic acids, mineral compounds and glycoproteins [5].

According to Polish Pharmacopoeia VI, the pericarp of *Phaseolus vulgaris* should contain not less than 0.01% of phenolic acids in conversion to caffeic acid [4]. *Phaseolus vulgaris* is mainly characterized by a diuretic effect, whose strength is proportional to the degree impairment of renal function. It also exerts antidiabetic activity [2, 6].

Long-term treatment with *Phaseoli pericarpium* extract was found to decrease significantly postprandial hyperglycemia and peripheral insulin resistance without affecting fasting glycemia [7].

Decoctions, infusions, teas and herbal mixtures of the extract are used in kidney diseases, urinary bladder, diminished urine excretion and edema due to water, chloride and sodium ion retention in the body. Toxic metabolic waste products are excreted through increased urine output, which supports the treatment of urolithiasis (particularly phosphate), inflammation of the urinary tract, gout and diabetes [8-10].

The following preparations containing *Phaseoli pericarpium* extract are available in Poland: Diabetofort (manufacturer: Leki Natury), Urosept (manufacturer: Herbapol Poznań), Diabetosan Fix (manufacturer: Herbapol Lublin), Glukostin-Hasco (manufacturer: Hasco-Lek), Vitalform (manufacturer: Legosan AB).

Current technology allows active complexes of substances to be obtained from dry titrated herbal extract (lipophilic-ethanol, hydrophilic-water). They are used as standardized formulations almost utterly devoid of ballast substances in the form of extracts used for the production of oral solid form of a drug [11].

At present, the most common route of drug administration is oral ingestion. More than 60% of all medicines offered by pharmaceutical industry are administered orally. Tablets are one of the most commonly used drug forms [12].

Only small number of therapeutic substances are capable of forming tablets under high pressure without the use of excipients. These substances are able to increase plastic deformation and tablet mass liquidity [13]. The Prosolv SMCC 50, PROSOLV EASYtab, EMDEX, Carmellose calcium and PRUV excipients were used in present study as carriers of dry *Phaseoli pericarpium* extract for direct compression.

To increase the surface area of microcrystalline cellulose for sorption, it can be covered by colloidal silicon dioxide to form silicified microcrystalline cellulose (SMCC). In this case the resulting new excipient was given the trade name Prosolv SMCC 50, and is composed of 98% of microcrystalline cellulose and 2% of colloidal silicon dioxide (SiO_2). It has improved binding and disintegrating properties, as well as flowability.

The use of this substance allows the tablets manufacturer by direct compression (excluding the granulation process) to increase the speed of production, to increase tablet hardness and to eliminate the controversial role of excipients, which automatically reduces the tablet size. Furthermore, by decreasing the use of binding substances, the production cost is reduced and thus, the efficacy of tablet compression is increased. It allows for precise distribution of the therapeutically active agent in the manufactured tablet and guarantees the increase of stability of the obtained drug form [14-17].

PROSOLV EASYtab is the trade name of an excipient containing 96% microcrystalline cellulose (binder), 2% colloidal silicon dioxide (glidant), 1.3% sodium starch glycolate (disintegrant) and 0.7% sodium stearyl fumarate (lubricant). This substance reduces the content of excipients in tablet manufacture allowing the amount of the therapeutic substance to be increased. Furthermore, the produced tablets are of the same mass, increased hardness and stability and disintegration time is significantly reduced. Prosolv EASYtab is a novel ready-to-use excipient mixture [18-20].

EMDEX is the trade mark of a binder used in the production of ingestible, chewable, soluble and effervescent tablets. It consists of 95% glucose, <2% gentobiose, <2% isomaltose, <1% maltose, <0.5% pentose, <0.1% maltotriose. The obtained tablets are characterized by high hardness [19].

Carmellose calcium, also known as carboxymethylcellulose calcium, and is used in the pharmaceutical industry as a coating agent, disintegrant and stabilizer. It is usually added in amount of 2 to 3% to the tablet mass and acts as a disintegrant in the direct compression process. If a larger amount is used, the disintegration time is prolonged [21].

Sodium stearyl fumarate (PRUV) is one of the excipients exhibiting gliding, anti-adhesive and lubricating properties. It is usually used in the process of tableting at a concentration of 0.5–2%. It is less popular than magnesium stearate, commonly used, but slows tablet disintegration to a lesser degree. It also allows tablets of very good hardness to be produced. Contrary to magnesium stearate, PRUV is a highly water-soluble excipient facilitating flowability, rapid disintegration and preventing tablet crushing [15, 22]. The use of direct compression without granulation is currently gaining popularity in the pharmaceutical industry, because it is simpler and more cost-effective from the point of view of good manufacturing practice (GMP). Hence, new formulations should be designed and the old ones should be modernized, as this will prove to be highly beneficial for many therapeutic substances [23]. The use of dry plant extracts in the process of direct compression without granulation decreases the possible loss of biological activity by the active agents [24]. As dry plant extracts are usually hygroscopic, which creates problems during direct compression, silicon dioxide is applied as a drying adjuvant [25].

Recently, greater use of tensides (surfactants), particularly non-ionic surface-active agents has been observed in the technology of solid oral dosage forms. Surfactants may be used as wetting agents in tablets containing a hydrophobic therapeutic agent, which leads to faster disintegration of the tablet and thus results in better pharmaceutical availability of the active component. The presence of the tenside in the tablet coating accelerates its disintegration.

The aim of this study is to produce a model drug form containing standardized dry *Phaseoli pericarpium* extract with compatible substances which provide desired tablet disintegration time, appropriate morphological properties and, what is most important, high pharmaceutical availability in model acceptor fluids. By examining the pharmaceutical availability of the substances during the study, our results will indicate the model formulation which will ensure appropriate therapeutic agent release and a high degree of mass exchange at the phase boundary, i.e. the first pass barrier. Non-ionic surfactants will be identified that improve the lithogenic index and at the same time reduce the amount of therapeutic agent adsorbed on the surface of the excipient [26]. Selected surfactants, cholesterol oxyethylenation products ($n_{TE} = 30$, $n_{TE} = 40$) and products of oxyethylenation of fatty acid methyl esters contained in pharmacopoeial rapeseed oil (Rofam $n_{TE} = 50$) [26, 27] were used in the study. Rofams belong to a new class of non-ionic tensides. The parameters given for each surfactant describe the average amount of oxyethylene segments, for instance $n_{TE} = 30$ indicates the amount of 30.

MATERIAL AND METHODS

Material

Dry extract of *Phaseoli pericarpium* (*extractum Phaseolus vulgaris e pericarpium aq. Siccum,* Phytopharm Klęka S.A.) was used for the study, with water as the extraction medium.

Data concerning the dry extract of *Phaseoli pericarpium* (*Extractum Pericarpium Phaseoli aq. siccum*) composition are as follows: 97% of native extract and 3% of colloidal silicon dioxide, with the content of phenolic acids in conversion to caffeic acid (active substances) tested according to the attached method (PRZ/003/02/2008) and extract identity confirmed according to the attached method (PRT/002/02/2008). Specification: EXTR. PHASEOLI. PERICARP. AQUOS. SICC.70% NATIV Martin Bauer Group ITEM 0173140 VERSION No. 13 REPLACES EDITION 11.05.2009 DATE 11.03.2010.

Excipients

The following excipients were obtained from JRS Rettenmaier (JRR Pharma, Germany): Prosolv SMCC 50 silicified microcrystalline cellulose, PROSOLV EASYtab, EMDEX and PRUV Sodium stearyl fumarate. Carmellose calcium USP/NF Disintegrant JP (CAS No. 9050-04-8) E.C.G®-505 (Lehmann & Voss & Co., Japan) was also used as an excipient.

The following homologous series of non-ionic surface-active agents were obtained from the ICSO Blachownia Surface-Active Agents Plant (Kędzierzyn Koźle, Poland): cholesterol oxyethylenation products $n_{TE} = 30$, HLB = 15.9 [26], cholesterol oxyethylenation products $n_{TE} = 40$, HLB = 16.5 [26], fatty acid methyl ester oxyethylation products of contained in pharmacopoeial rapeseed oil Rofam $n_{TE} = 50$, HLB = 17.1 [27].

Reagents

The following reagents were used: water purified according to Eur Ph 7; artificial enzyme-free gastric juice (0.1 mol/l aqueous solution of hydrochloric acid (HCl); artificial enzyme-free intestinal juice (phosphate buffer solution of pH = 6.8). In addition, analytical grade sodium hydroxide and analytical grade potassium dihydrogen phosphate were obtained from POCh, Gliwice, Poland.

Apparatus

Korsch EK-O type reciprocating instrumented tableting machine (Erweka GmbH, Germany); ZT 222 apparatus for testing disintegration rate (Erweka GmbH, Germany); DT 606/1000 HH, apparatus for testing the rate of therapeutic agent release from the drug form (Erweka); TAR 220, friability/abrasion tester (Erweka GmbH, Germany); Nicolet Evolution 300 UV-VIS spectrophotometer, Spectro-Lab (Warszawa, Poland) with PC control and Excel spreadsheet (Microsoft). In addition, the following laboratory equipment was used: a sieve with 0.7 mm mesh

diameter, electronic balance, Radwag (Radom, Poland), electronic slide caliper Mitutoyo, Type CD-15CP, Japan.

Technology of model tablet manufacturing

In the first stage, four batches of tablets were manufactured, each tablet containing 50% *Phaseoli pericarpium* extract (250 mg) with 49% fillers and disintegrants (Prosolv SMCC 50, PROSOLV EASYtab, EMDEX, Carmellose calcium) and 1% PRUV lubricant. In the second stage, an oral solid dosage form was manufactured on the basis of the batch 1 tablet formulation (extract, Prosolv SMCC 50, PRUV) and 1% different surfactants were successively added (cholesterol oxyethylate n_{TE} = 30, cholesterol oxyethylate n_{TE} = 40, Rofam n_{TE} = 50) to obtain three batches of tablets. The composition of individual batches is specified in table 1. All components were weighed per adequate number of tablets (500 mg each).

Table 1.

Tablet composition

Tablet composition	Batch number						
	1	2	3	4	1A	1B	1C
Phaseoli pericarpium extract	+	+	+	+	+	+	+
Prosolv SMCC 50	+				+	+	+
PROSOLV EASYtab		+					
EMDEX			+				
Carmellose calcium				+			
Cholesterol oxyethylate n_{TE}=30					+		
Cholesterol oxyethylate n_{TE}=40						+	
Rofam n_{TE}=50							+
PRUV	+	+	+	+	+	+	+
Tablet mass, mg	500	500	500	500	500	500	500

A dry mixing technique was used to produce the tablet mass, and the extract was blended with excipients. The obtained mass was sieved through a 0.7 mm mesh screen, and compressed using a press tablet machine (Erweka) with an Ø11 mm punch. PRUV was used as a lubricant to manufacture all 7 tablet batches: it inhibits the tablet disintegration rate to a lesser extent than magnesium stearate while improving tablet hardness. The manufactured uncoated tablets were tested, and their therapeutic utility was determined.

Morphological tests of tablets with dry extract from *Phaseoli pericarpium*

The disintegration time of the tablets was determined according to the European Pharmacopoeia 7 [28]. Water, artificial gastric and intestinal juice were used as acceptor fluids.

The tablets were also tested for their appearance (size), dosage accuracy (determination of the mass uniformity of individual tablets) and mechanical resistance (abrasiveness). The hardness of the manufactured tablets was also analysed statistically. The methodology of the study, the size of samples collected for analysis and the limits of acceptable deviation from the expected standard were based on the general and detailed principles of the Eur Ph 7 [28].

Examination of biologically-active substance content

The actual dose was determined by measuring the active substance content in the tablet. Ten tablets were randomly chosen, weighed and pulverized in a mortar. The resulting powder was prepared for analysis. The corresponding unit weight of the tablet was measured, and the amount of the biologically active substances was determined.

Testing the pharmaceutical availability of active substances from tablet to acceptor fluid

The pharmaceutical availability of biologically active substances from tablets was determined in a dedicated apparatus for measuring therapeutic substance release according to the rotating basket method, in accordance with the Eur Ph 7 [28]. Three types of acceptor fluids were used: water, artificial gastric juice, artificial intestinal juice (enzyme-free, degassed). The dependence of absorbance (A) on concentration function (c) was described with a correlation equation, with a determination coefficient $R^2 > 0.9990$ obtained at a level of significance of $p = 0.05$ (tab. 2). The concentration of the released biologically active substances from the obtained tablets to acceptor fluid was determined using a UV spectrophotometer ($\lambda = 268$ nm) at a temperature of $37 \pm 0.5^{\circ}$C. The sample volume was 10 ml. The acceptor phase consisted of purified water, artificial gastric juice, or artificial intestinal juice. Tablets manufactured only from excipients were used as a reference material. Calibration curves were constructed to quantify the dissolution and diffusion of the sum of biologically active substances to the model acceptor fluids. The results were analysed with the use of Microsoft Excel spreadsheet.

Table 2.

Calibration curve equations for three measurement systems of acceptor fluids: water, artificial gastric juice and artificial intestinal juice

Type of acceptor fluid	Determination coefficient (R^2)	Wave length [nm]	Correlation equation
Water	0.9992	268	$A = 1.9705 \times c$
Artificial gastric juice	0.9992	268	$A = 1.5433 \times c$
Artificial intestinal juice	0.9990	268	$A = 1.7583 \times c$

A – absorbance of biologically active substances for the reference solution,
c – the concentration of the extract of the standard solution [mg/100 ml].

Ethical approval: The conducted research is not related to either human or animal use.

RESULTS AND DISCUSSION

Assessment of the quality of tablets containing dry *Phaseoli pericarpium* extract

The physicochemical properties of the tablets are specified in table 3.

As carriers of dry *Phaseoli pericarpium* extract, the applied excipients were found to supplement the process of direct tableting. The tablets manufactured within each of seven batches demonstrated a smooth surface with no stains, a uniform shape and yellow color originating from the extract. Low values of deviation from the mean mass (tab. 3) indicated high uniformity of tablet mass. No chips or mechanical defects were present, which was confirmed by testing the mechanical resistance to abrasion: the loss of total mass did not exceed 1%. The abrasiveness oscillated from 0.03 to 0.40%. The highest abrasiveness values were found in the tablets incorporating Carmellose calcium and PRUV (batch 4). The tablets may be considered sufficiently resistant to crushing because the hardness coefficient T was greater than 98 N/cm^2 for all 7 batches of tablets. The hardness of the designed tablets ranged from 119.5 to 268.3 N/cm^2. The greatest hardness was observed for batch 1B, which contained Prosolv SMCC 50, Oxyethylate n_{TE} = 40 and PRUV. Furthermore, these tablets demonstrated low abrasiveness of 0.07%. The lowest hardness of 119.5 N/cm^2 was noted for batch 4 tablets, which, as it was noted above, were also characterized by the highest abrasiveness (0.4%).

The similar tablet density values observed in all batches confirm that the substances used for tablet manufacturing are homogeneous. This is also confirmed by the calculated mean tablet surface values (tab. 3). Minimal differences were found between the diameter of the tablets from individual batches and the diameter of the punch points to low tension in the tablet pulled out of the matrix.

Table 3.

Tablet physicochemical properties

Parameter		Batch							Norm
		1	2	3	4	1A	1B	1C	
Mean mass [mg]		500.0	500.1	500.4	500.0	500.1	500.0	500.0	500.0
Deviation from mean mass, %		0.39	0.30	0.37	0.32	0.42	0.39	0.51	< 5.0
Content of biologically active substances ±SD		100.2 ± 0.5	100.5 ± 0.8	99.2 ± 0.9	98.8 ± 1.5	101.0 ± 1.2	100.8 ± 0.9	99.5 ± 0.7	100.0
Mean tablet diameter [cm]		1.106	1.105	1.105	1.116	1.102	1.104	1.103	1.100
Mean tablet height [cm]		0.47	0.45	0.44	0.49	0.46	0.45	0.43	–
Mean tablet surface [cm^2]		3.56	3.48	3.46	3.67	3.52	3.50	3.41	–
Disintegration time [min]	Water	19	20	6	11	18	19	23	15
	Artificial gastric juice	20	21	8	12	20	23	21	15
	Artificial intestinal juice	20	23	7	10	19	20	18	15
Mean tablet density [g/cm^3]		1.108	1.159	1.186	1.044	1.140	1.161	1.213	–
Abrasiveness F, %		0.06	0.03	0.25	0.40	0.12	0.07	0.10	< 1.0
Hardness [N/cm^2]	T (x^-)	197.1	261.3	197.5	119.5	226.2	268.3	246.0	> 98
	± dT	8.52	9.87	19.63	22.46	11.09	15.61	18.15	–

The combination of high hardness values and low abrasiveness (predisposition to crushing) indicates that the tablets can be easily packed into blisters. This formulation ensures morphological durability as the tablet is pulled out from the blister niche.

The process of disintegration was uniform for tablets from all seven batches, with the disintegration time ranging between 6 and 23 minutes. In general, batch 3 tablets (EMDEX, PRUV, *Phaseoli pericarpium*) demonstrated the shortest disintegration time to all three normative acceptor fluids, the shortest of which was to water (6 min) followed by artificial intestinal juice (7 min) and artificial gastric juice (8 min). The addition of surfactants to the tablets (hydrophilizing agents HLB=15–17) slightly increased their hardness as compared to that of the batch 1 tablets without surfactants. However, this change did not affect the disintegration time of the tablets, which was comparable to that of the batch 1 tablets. This could have been caused by the low ability of substances used for tablet manufacture to reduce the surface tension and phase boundary tension.

The rate of active substance release

The pharmaceutical availability of the biologically active substances from the tested tablets was determined according to the requirements of the Eur Ph 7 [28]. Three types of acceptor fluids recommended by Pharmacopeia were used: water, artificial gastric juice and artificial intestinal juice.

In figure 1 the effectiveness of the release of biologically active substances from individual tablet batches to the acceptor fluid (water) was compared. Batch 4 tablets containing Carmellose calcium as a dominant carrier released the least biologically active substances, obtaining a maximum of 87.2% after 30 min. The release of active substance from batch 2 tables, containing PROSOLV EASYtab, was worse than that of batch 4 tablets: a slow increase of active substance release could be observed in 60 min. The maximum release value was 102.4% after 240 minutes. Batch 3 tablets, containing EMDEX, initially released biologically active substances in a similar way to batch 2 tablets, obtaining a maximum value of 77% after 90 minutes. Further stabilization was observed and then release was slightly decreased. In the case of batch 1 tablets, Prosolv SMCC 50 was used as a main carrier of *Phaseoli pericarpium* extract. At the beginning of the process of release, this batch exhibited the least pharmaceutical availability: the maximum value of the released active substances, being 75.2% after 150 minutes (fig. 1). This batch of tablets also demonstrated the lowest release to artificial gastric juice (83.6%, fig. 2), and to artificial intestinal juice (70.8%, fig. 3), as compared to other tablet batches produced during the first stage of the study.

Therefore, to improve pharmaceutical availability, three tablet batches (1A, 1B, 1C) were produced on the basis of the batch 1 tablets (dry *Phaseoli pericarpium* extract, Prosolv SMCC 50, PRUV by adding successively different surfactants (cholesterol oxyethylate $n_{TE}=30$, cholesterol oxyethylate $n_{TE}=40$, Rofam $n_{TE}=50$). The introduction of 1% of surfactants (batch 1A, 1B, 1C) resulted in a slight increase of pharmaceutical availability to water at the beginning of the process of active substance release compared to batch 1 tablets.

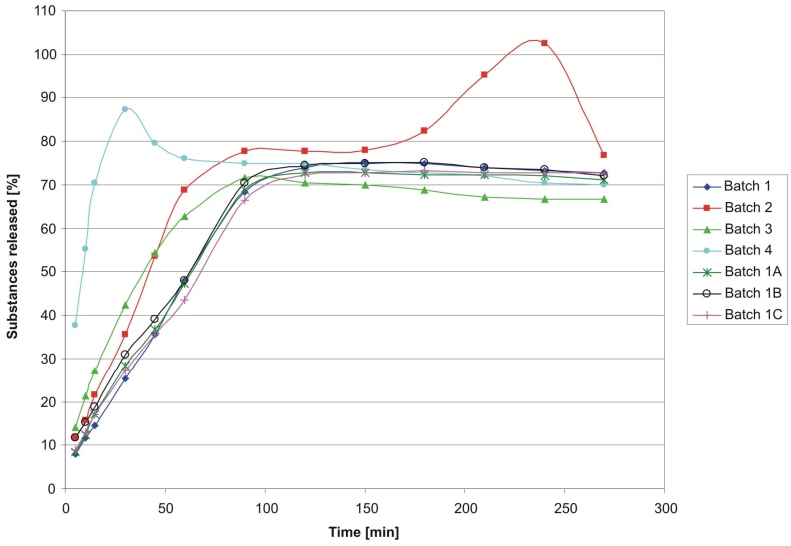

Figure 1.

Profiles of the release of biologically active substances from tablets to water (batch 1–4, 1A, 1B, 1C)

Figures 2 and 3 specifies the profiles of biologically active substance release from batch 1 tablets to artificial gastric juice and artificial intestinal juice. The release of biologically active substances from batch 1A, 1B and 1C tablets to artificial gastric juice or to artificial intestinal juice was found to be significantly greater than that demonstrated by batch 1 at the beginning of the release process. For the artificial gastric juice, the maximum quantity of the released active substances was 88.4% for batch 1B, containing cholesterol oxyethylate n_{TE} = 40, 88.8% for batch 1A with cholesterol oxyethylate n_{TE}=30, and 89.6% for batch 1C with Rofam n_{TE}=50. These values were higher than that of the batch 1 tablets (83.6%). The maximum release of therapeutic substances to artificial intestinal juice was 78.8% for batch 1A, 78.8% for batch 1C, 99.2% for batch 1B. These values were also higher than those observed for batch 1 tablets, for which the maximum pharmaceutical availability to artificial intestinal juice was 76.8%.

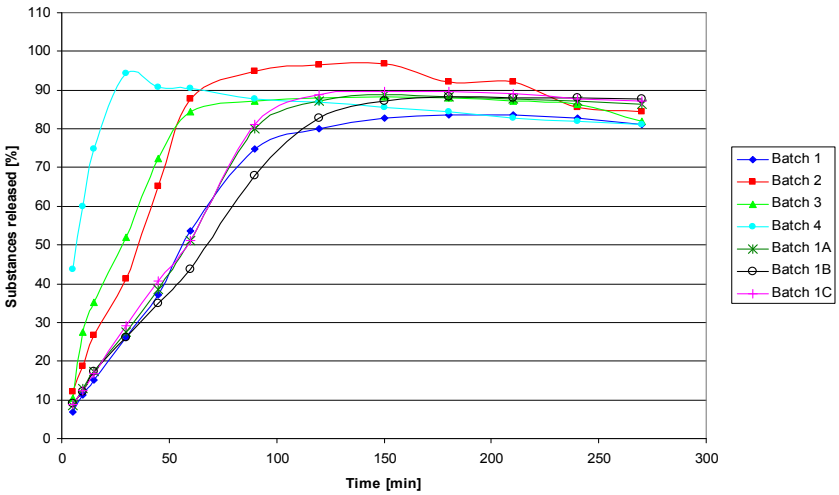

Figure 2.

Profiles of the release of biologically active substances from tablets to artificial gastric juice (batch 1–4, 1A, 1B, 1C)

It was also indicated that batch 4 tablets, including Carmellose calcium in their composition, released most of their biologically active substances into the external compartment (water, artificial gastric juice and artificial intestinal juice). This batch released the substances slower, i.e. 30 min after other batches.

Despite lacking surfactants, batch 2 tablets containing PROSOLV EASYtab, an innovative mixture of ready-to-use excipients, released the highest amount of biologically active substances to water and artificial intestinal juice, however, in longer time.

The release curve profiles indicated the incomplete release of biologically active substances (i.e. less than 100%). This confirms that sorption of active substances by formulation components was taking place.

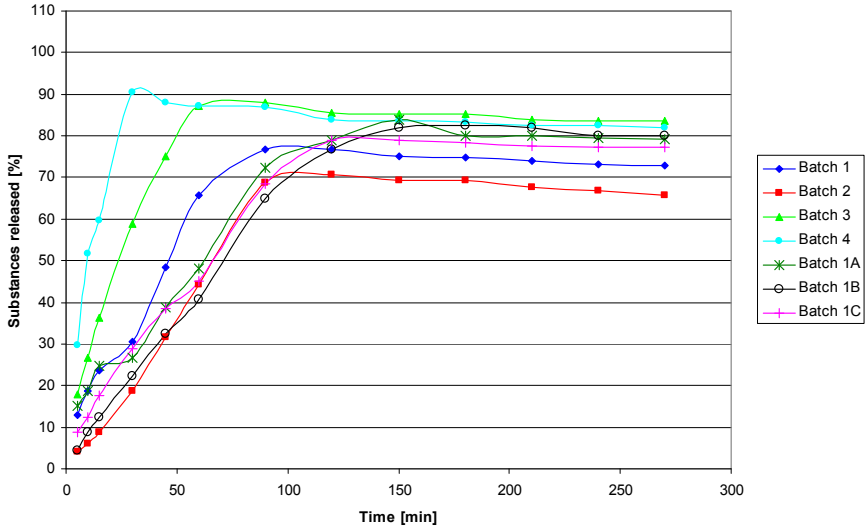

Figure 3.

Profiles of the release of biologically active substances from tablets to artificial intestinal juice (batch 1–4, 1A, 1B, 1C)

Summing up, it can be stated that the presented method of manufacturing a solid dosage containing dry *Phaseoli pericarpium* extract is optimal, ensures technological repeatability and high durability of suggested form. The method of direct compression is cost- and time-effective, as compared to wet granulation.

The obtained tablets can act as supplements for medications for kidney, urinary tract and urinary bladder diseases, as well as in diabetes. The recommended dosage may be 1 tablet containing 250 g of dry extract of *Phaseoli pericarpium* 3 to 4 times daily.

CONCLUSIONS

1. Application of selected excipients (Prosolv SMCC 50, PROSOLV EASYtab, EMDEX, Carmellose calcium) as dominating carriers of dry *Phaseoli pericarpium* extract allows to obtain, by direct compression method, tablets of physicochemical parameters complying with the requirements of European Pharmacopoeia 7.
2. The used surfactants allowed to manufacture tablets with dry *Phaseoli pericarpium* extract of more beneficial release profile of biologically active substances compared to batch 1 tablets which did not contain surfactants in their composition.

3. Addition of surfactants to the tested tablets increased their hardness a little, compared to batch 1 tablets without surfactants. However, this change did not affect significantly the tablet disintegration time.
4. Tablets containing Carmellose calcium in their composition released the highest quantity of biologically active substances to the external compartment: water, artificial gastric juice, artificial intestinal juice.
5. Analysis of the obtained results has confirmed that it is possible to apply the worked out technology for manufacturing an oral solid dosage form containing dry extract and its use in the production for a large scale.

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WYBRANE SUBSTANCJE POMOCNICZE I SURFAKTANTY W STAŁEJ DOUSTNEJ POSTACI LEKU ZAWIERAJĄCEJ EKSTRAKT Z OWOCNI FASOLI (*PHASEOLUS VULGARIS* L.)

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Streszczenie

Wstęp: Fasola zwyczajna (*Phaseolus vulgaris* L.) to roślina jednoroczna. Jest uprawiana w wielu krajach świata, w tym również w licznych odmianach w Polsce. Surowcem zielarskim są wydłużone strąki fasoli – owocnia. Owocnia fasoli obniża poziom cukru we krwi. Wyciągi ze strąków fasoli mają działanie moczopędne, mogą być używane w leczeniu obrzęków, chorobach nerek ze zmniejszonym wydalaniem moczu, kamicy nerkowej. **Cel**: Celem pracy było zbadanie przydatności wybranych substancji pomocniczych jako nośników suchego mianowanego ekstraktu z owocni fasoli zwyczajnej (*Phaseolus vulgaris* L.) **Metody**: Zastosowano metodę bezpośredniego tabletkowania. W dalszym etapie otrzymane tabletki poddano odpowiednim badaniom. Pierwszy etap pracy to ocena takich substancji jak Prosolv SMCC 50, PROSOLV EASYtab, EMDEX, Carmellose calcium, PRUV. Użyto ich do wykonania 4 serii tabletek. Drugi etap to wykonanie stałej doustnej postaci leku na bazie składu formulacyjnego tabletek serii 1 (wyciąg z owocni fasoli zwyczajnej, Prosolv SMCC 50, PRUV). Dodano do niego dodatkowo kolejno różne surfaktanty (cholesterol oxyethylate n_{TE}=30, cholesterol oxyethylate n_{TE}=40, Rofam n_{TE}=50), uzyskując 3 serie tabletek. Tabletki wszystkich 7 serii wykonano w tabletkarce uderzeniowej firmy Erweka. Następnie poddano je badaniom morfologicznym, ocenie właściwości fizykochemicznych, a także zbadano profile uwalniania substancji biologicznie czynnych do 3 wybranych płynów biorczych (woda, sztuczny sok żołądkowy, sztuczny sok jelitowy) zgodnie z wymogami przepisów ogólnych i szczegółowych monografii Farmakopei Europejskiej 7 (Eur Ph 7). **Wyniki**: Otrzymane tabletki miały gładką, jednolitą powierzchnię bez plam, odprysków i uszkodzeń mechanicznych. Charakteryzowały się żółtym kolorem pochodzących z ekstraktu. Tabletki posiadające w swoim składzie surfaktanty odznaczały się nieznacznie lepszą dostępnością farmaceutyczną w stosunku do tabletek serii 1 bez surfaktantów. **Wnioski**: Zastosowane substancje pomocnicze w odpowiednich proporcjach okazały się przydatne do wytworzenia tabletek niepowlekanych, zawierających wyciąg z owocni fasoli zwyczajnej.

Słowa kluczowe: *Phaseolus vulgaris, bezpośrednie tabletkowanie, surfaktanty, substancje pomocnicze*