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EXPERIMENTAL PAPER

Formulation and profile of pharmaceutical availability from a model oral solid form of a drug of phytochemicals contained in dry *Taraxacum officinale* extract

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S u m m a r y

Introduction: Dandelion (*Taraxacum officinale* coll.), also called the common dandelion grows wild throughout Europe, Asia and the Americas. It is a perennial plant of the family

of *Asteraceae*, having powerful healing properties. The entire plant – flowers, roots and leaves – is the medicinal raw material. **Objective:** The aim of this study was to manufacture model tablets of pharmacopoeial disintegration time by direct compression of dry titrated extract of dandelion with selected excipients. **Methods:** Tablets were obtained by direct compression using reciprocating tableting machine (Erweka). Morphological parameters – hardness, friability, disintegration time in pharmacopoeial acceptor fluids were investigated using Erweka equipment. Their actual surface area was also calculated. There was also tested the rate of dissolution of phytochemicals from model tablets in the presence of excipients in pharmacopoeial acceptor fluids (V=1.0 dm^3) by the method of a basket in Erweka apparatus. Spectrophotometric determinations were performed. **Results:** It results from the morphological studies of model tablets containing *Ext. Taraxaci e radix cum herba aqu. siccum* that they are characterized by comparable surface and friability at varying hardness, the latter depending on the applied excipients. This is reflected in the effective disintegration time in model acceptor fluids consistent with pharmacopoeial requirements. **Conclusions:** The used excipients enabled to produce model tablets containing dry extract of dandelion by direct compression. The obtained results demonstrated that microcrystalline Prosolv-type cellulose, Vivapur 200 and Emdex were compatible with the structure of the extract of dandelion. They allow to manufacture a model solid oral dosage forms of the desired morphological parameters and effective disintegration time complying with the pharmacopoeial requirements.

Key words: *Taraxacum officinale, direct compression, solubilization, solubility of phytochemicals, pharmaceutical availability*

INTRODUCTION

Preformulation studies indicate that the phytochemicals of dry extract of dandelion root (*Extractum Taraxaci e radix cum herba aqu. siccum*) can form non-ideal solutions in model acceptor fluids and reduce the surface tension (γ_{rz}) at the phase boundary [1]. The surface activity of aqueous solutions of the extract, as well as its estimated solubilizing capabilities relative to granular cholesterol ($HLB_{1HNMR} \approx 1.0$) of Ø = 1.00 mm and the ketoprofen technological crystallographic form, suggest that the technological preparation of dry extract does not degrade the structure of natural surfactants and that the micellar solubilization equilibrium is effective, despite the presence of chlorophyll [1]. Lipophilic structures of phytochemicals are hydrophilized in the extract by a glycosidic bond with sugar alcohols or by physicochemically-complex hydrotropic solubilization [2-4].

Direct compression using low surface adsorption capacity excipients (Freundlich adsorption isotherm) in model acceptor fluids was found to be the most suitable method for the production of a model solid form of a drug incorporating the phytochemicals from dry dandelion extract (*Ext. Taraxaci e radix cum herba aqu. siccum*) [5-7].

The aim of the study was to determine the relationship between the rates of the symmetrical processes of tablet disintegration and phytochemical dissolution in model acceptor fluids with excipients, wherein the concentration of saponins was lower than the critical micelle concentration (cmc); $c_{pom} \leq cmc$.

The study evaluates the morphological parameters of the produced solid oral dosage form. It also determines the pharmaceutical availability of the phytochemicals in three model acceptor fluids: water, 0.1 mol HCl and phosphate buffer at pH=6.88. The obtained results allowed the pharmaceutical availability of phytochemicals to be mathematically modelled for *in vitro* assessment [8, 9, 10].

The results will enable the production of a pharmacotherapeutically effective form of drug that can be used in the treatment of, *inter alia*, bile and gall bladder diseases [11-14].

MATERIAL AND METHODS

Plant material

- Dry extract from dandelion root and herb – *Extracum Taraxaci radix cum herba aqu. siccum*; Phytopharm Klęka, S.A., Poland
- Prosolv SMCC 50 – JRS Pharma, Germany
- Prosolv SMCC 90 – JRS Pharma, Germany
- Prosolv HD 90 – JRS Pharma, Germany
- Vivapur 200 – JRS Pharma, Germany
- EMDEX – JRS Pharma, Germany
- Vivasol – JRS Pharma, Germany
- Sodium stearyl fumarate (PRUV) – JRS Pharma

Acceptor fluids

- distilled water, 0.1 mol/l hydrochloric acid of declared osmolarity 200 m Osm/l analytical grade, CHEMIPUR, Piekary Śląskie, Poland
- phosphate buffer, pH=6.88 (composition: water, sodium hydroxide, analytical grade), CHEMIPUR, Piekary Śląskie, Poland
- monobasic potassium phosphate analytical grade, P.P.H POCh Gliwice, Poland

Apparatus

- Reciprocating instrumented tableting machine: Korsch EK-O, Erweka, Germany
- Apparatus for testing tablet abrasiveness (friabilator): Erweka Tar 220, Germany
- Apparatus for testing the rate of release of biologically active agents from a tablet: Erweka DT 606/1000 HH, Germany
- Apparatus for testing tablet disintegration rate: Erweka ZT 606/1000 HH, Germany
- Hardness tester: Erweka TBH-200 TD, Germany

- UV/VIS Spectrophotometer with computer control system: Nicolet Evolution 300, Thermo Electron Corporation
- Digimatic caliper: Mitutoyo, CD-15.

The manufacture and morphological parameters of model uncoated tablets containing dry aqueous extract from dandelion root and herb (*Ext. Taraxaci radix cum herba aqu. siccum*)

The tablet mass was prepared by mixing. The tablet ingredients were added to a high-speed mixer (Fukae Powtec) containing the conversion amount of dandelion root, herb extract and lubricant (sodium stearyl fumarate, PRUV) through a Ø=0.16 mm sieve. The tablet mass was stirred for 20 min and passed again through a Ø=0.25 mm sieve. The model tablets themselves were manufactured by direct compression, and their hardness, abrasiveness, disintegration rate in model acceptor fluids and actual surface area was calculated (in mm^2). The composition of the model formulations (No. 1-3) [15-22] and their morphological parameters are presented in table.

Profiles of pharmaceutical availability of phytochemicals from a model tablet in pharmacopoeial acceptor fluids

The rate of dissolution of phytochemicals from the model tablets in the presence of excipients was tested in 1.0 dm^3 pharmacopoeial standard acceptor fluid by the basket method [23]. The concentration of the natural surfactants (saponins) was therefore significantly lower than that of cmc; $c_{exp} << cmc$.

Samples of 10.0 cm^3 were taken, passed through Millipore filters and subjected to spectrophotometric determination at $\lambda_{max}=291$ nm. A calibration curve was determined based on the spectrophotometric characteristics of dry *Ext. Taraxaci e radix cum herba aqu. siccum*.

The amount of phytochemicals dissolved in the acceptor fluid, with respect to time (~t; min), was calculated based on the following approximation equations:

- for water (A=f(c), y=a·x) at $p=0.05$ and $r^2=0.9998$, y=2.4634·c,
- for 0.1 mol HCl (A=f(c), y=a·x) at $p=0.05$ and $r^2=0.9995$, y=2.1576·c
- and for phosphate buffer of pH=6.88 (A= f(c), y=a+b·x) at $p=0.05$ and $r^2=0.9998$, y=2.4711·c to the form c=y/a.

The result of these equations is the release coefficient Q (%). The coefficient acts as the basis for the kinetic models used to reliably estimate the dynamics of phytochemical dissolution in the presence of excipients and in pharmacopoeial acceptor fluids. The profiles of phytochemical release to the acceptor fluids may then be traced thus: Q (%) = f (t, minutes).

Kinetic models of pharmaceutical availability of phytochemicals

The process of pharmaceutical availability in model tablets occurs symmetrically to the integration process, and correlates with the maximal surface of the tablet mass in acceptor fluid. Therefore, the complex process of dissolution of phytochemicals in the absence of effective micellar solubilization (c_{exp} saponin $<<$cmc) was described by mechanistic models based on Fick's equation, and kinetic models based on physical laws. Hence, the following model equation systems were used to describe the rate of dissolution:

(1) $Q(\%)=f(t, \text{minutes})$; $Q(\%)=a+k\cdot t$
(2) $\log Q(\%)=f(t, \text{minutes})$; $\log Q(\%)=a+k\cdot t$
- kinetics of zero and first order,
(3) $Q(\%)=f(\sqrt{t})$; Higuchi model $Q(\%)=k\cdot t^{1/2,}$
which is the base for Fick's diffusion model,
(4) $\log Q(\%)=f(\log t)$ – Krosmeyer-Peppas model
$Q(\%)=k\cdot t^{n}$ which, in a logarithmic system, assumes the form
$\log Q= \log k +n \log t$ (in application, $\log Q=a+n \log t$ is used;
where $a=\log k$),
(5) $Q_o^{1/3}(\%)-Q_o^{1/3}(\%)=K_H\cdot t$ – Hixon-Crowell model, which in application, assumes the form:
$\sqrt[3]{100}-Q_t(\%)=f(t, \text{min})$.

In zero-order and first-order kinetic models, the rate of release of phytochemicals is assumed to be independent of the function of time (t, minutes). However, in the Krosmeyer-Peppas model and Higuchi model, which assume that the process of release is consistent with Fick's law, the rate of release (dissolution) of phytochemicals varies in time.

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

RESULTS AND DISCUSSION

The morphological studies (tab. 1) indicate that the tablets are characterized by comparable surface and abrasiveness at varying hardness, which is an effect of the granulometric properties of the excipients. This is reflected in the effective disintegration time in the model acceptor fluids: the process of disintegration lasts no longer than 13.5 minutes, thus meeting the pharmacopoeial requirements.

The process of tablet disintegration and the rate of phytochemical dissolution in water against time (tab. 2) revealed that after their effective disintegration, the concentration of soluble phytochemicals (approximately 15-minute exposure) did not exceed $Q(\%)\approx 50\%$. Longer exposure favored solubility, which, for the formulation F-1 $\sim$ F-4, reached a value higher than $Q(\%)\approx 90\%$. Only formulation with EMDEX decreased the effective solubility of the phytochemicals (tab. 3, 4).

Table 1.

Formulation composition and selected morphological parameters of model tablets containing *Ext. Taraxaci e radix cum herba aqu. siccum*

Therapeutic agent / Excipients	Formulation No 1	Formulation No 2	Formulation No 3	Formulation No 4	Formulation No 5
1. *Ext. Taraxaci e radix cum herba aqu. siccum*	0.150	0.150	0.150	0.150	0.150
2. Prosolv SMCC50	+	–	–	–	–
3. Prosolv SMCC 90	–	+	–	–	–
4. Prosolv HD 90	–	–	+	–	–
5. Vivapur 200	–	–	–	+	–
6. EMDEX	–	–	–	–	+
7. Vivasol	+	+	+	+	–
8. Sodium stearyl fumarate	+	+	+	+	+
Height – n [nm]	3.71	3.51	3.51	3.51	3.42
Diameter – d=2r [mm]	10.05	10.04	10.04	10.07	10.06
Real surface [mm^2]	275.62	268.90	268.90	270.17	266.91
Hardness [N/cm^2]	105.3	110.2	120.8	50.6	189.4
Abrasiveness [%]	0.09	0.28	0.14	0.49	0.22
Disintegration time [min]					
– in water	10.28	12.11	13.08	12.24	10.30
– in 0.1M HCl	11.28	14.30	15.30	14.25	12.12
– in buffer (pH=6.88)	11.24	12.09	13.28	12.38	11.28
m_t – mean tablet mass	300±0.40	300±0.47	300±0.77	300±0.58	300±0.47

Table 2.

Velocity of phytochemicals' disintegration in water according to time function

Exposure time t [min]	$\sqrt{t}$	Medium: water: Q – of released phytochemicals				
		Formulation No. 1	Formulation No. 2	Formulation No. 3	Formulation No. 4	Formulation No. 5
1.5	1.22	7.31	15.16	4.33	14.07	5.41
3.0	1.73	15.70	20.30	23.82	15.97	12.18
4.5	2.12	18.67	33.56	26.25	18.40	12.99
6.0	2.45	22.46	35.45	30.31	20.30	15.70
9.0	3.00	25.98	38.70	36.81	26.52	18.94
12.0	3.46	31.39	44.11	44.92	30.04	20.57
15.0	3.87	39.78	49.80	49.17	35.45	24.63
20.0	4.47	46.82	54.13	56.56	48.17	31.66
25.0	5.00	59.54	62.24	71.45	54.40	35.99
30.0	5.48	78.21	75.51	86.33	65.76	40.32
35.0	5.92	84.17	84.44	89.85	74.69	44.38
45.0	6.71	92.01	96.61	94.72	85.79	52.50
60.0	7.75	93.37	97.70	94.45	88.77	63.87
90.0	9.49	92.83	95.53	93.91	90.39	73.61
120.0	10.95	92.83	95.80	93.10	90.66	76.86

Table 3.

Velocity of phytochemicals' disintegration in HCl according to time function

Exposure time t [min]	$\sqrt{t}$	Medium: 0.1 mol HCl; Q – of released phytochemicals				
		Formulation No 1	Formulation No 2	Formulation No 3	Formulation No 4	Formulation No 5
1.5	1.22	3.40	5.87	3.71	9.27	5.25
3.0	1.73	8.96	7.11	7.11	13.60	9.28
4.5	2.12	9.58	7.72	8.03	17.92	11.12
6.0	2.45	12.36	10.51	9.27	20.70	14.21
9.0	3.00	16.69	14.83	12.67	25.34	15.45
12.0	3.46	19.78	21.94	17.30	29.35	18.23
15.0	3.87	23.17	26.57	22.25	33.06	21.01
20.0	4.47	31.52	29.97	26.26	38.01	26.26
25.0	5.00	41.41	34.92	33.99	46.97	32.14
30.0	5.48	48.51	38.62	37.08	52.53	35.84
35.0	5.92	57.78	43.26	45.11	63.04	38.93
45.0	6.71	67.98	67.98	55.93	72.92	47.28
60.0	7.75	77.56	77.25	72.00	78.79	60.25
90.0	9.49	84.05	82.14	80.34	82.19	72.00
120.0	10.95	87.14	63.74	83.12	84.05	77.56

Table 4.

Velocity of phytochemicals' disintegration in phosphate buffer according to time function

Exposure time t [min]	$\sqrt{t}$	Medium: phosphate buffer pH = 6.88; Q – of released phytochemicals				
		Formulation No 1	Formulation No 2	Formulation No 3	Formulation No 4	Formulation No 5
1.5	1.22	9.98	16.19	4.86	9.17	2.16
3.0	1.73	11.87	19.16	11.60	17.54	8.09
4.5	2.12	15.11	24.82	15.38	18.08	11.87
6.0	2.45	18.89	30.22	20.23	22.66	14.57
9.0	3.00	22.93	35.07	22.93	28.87	15.45
12.0	3.46	28.33	40.47	26.98	34.53	18.35
15.0	3.87	35.61	48.29	29.41	37.77	21.85
20.0	4.47	45.32	60.97	40.20	49.64	27.25
25.0	5.00	54.77	67.45	44.52	57.47	31.03
30.0	5.48	65.83	73.11	52.88	64.75	35.07
35.0	5.92	70.68	79.05	61.24	74.46	40.20
45.0	6.71	80.40	84.44	75.54	83.63	48.56
60.0	7.75	82.29	84.17	82.02	85.79	60.16
90.0	9.49	82.29	84.17	85.79	87.95	74.73
120.0	10.95	81.21	83.63	85.25	87.95	78.24

However, although the solubility value decreased to Q(%)≈80% in 0.1 mol HCl and phosphate buffer at pH=6.88, the value did not exceed Q(%)≈78.5% for the formulation with EMDEX. This is due to the hydrolysis of glycosidic bonds, the lack of effective hydrotropic solubilization in pharmacopoeial acceptor fluids of high osmolarity and the varied activity of hydrogen ions: pH(a_{H+}) ranging from

approximately 1.86 to 6.88. These values confirm that microcrystalline cellulose (silicified SiO_2), Prosolv and Vivapur-type are compatible excipients for dry *Ext. Taraxaci e radix cum herba aqu. siccum* tableting [4] (tab. 1, fig. 1, 2, 3).

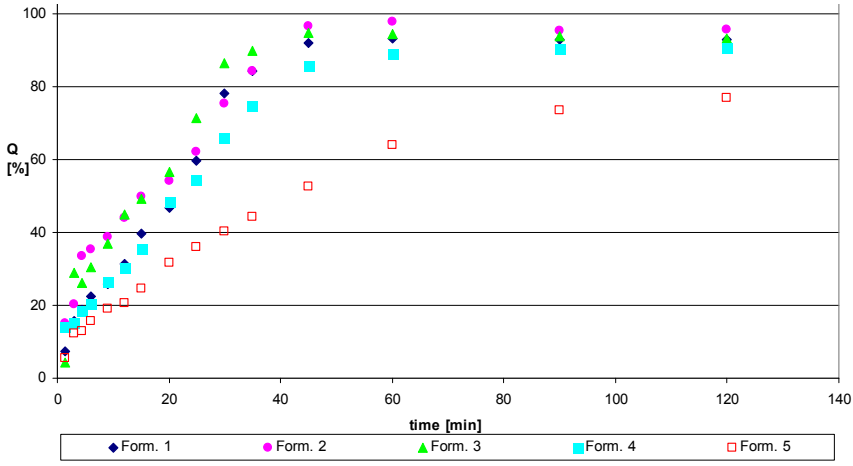

Figure 1.

Relationship between amount of released substance Q% with time (t) for water as medium

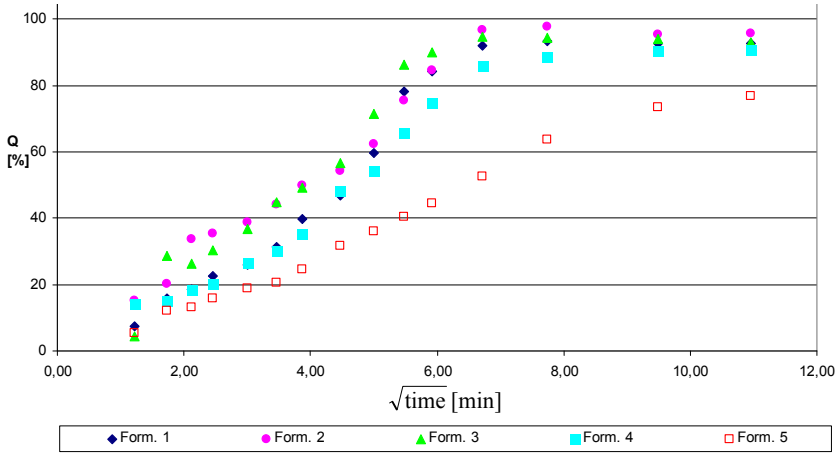

Figure 2.

Relationship between amount of released phytochemicals Q% with time ($\sqrt{t}$) in Higuchi model for water as medium

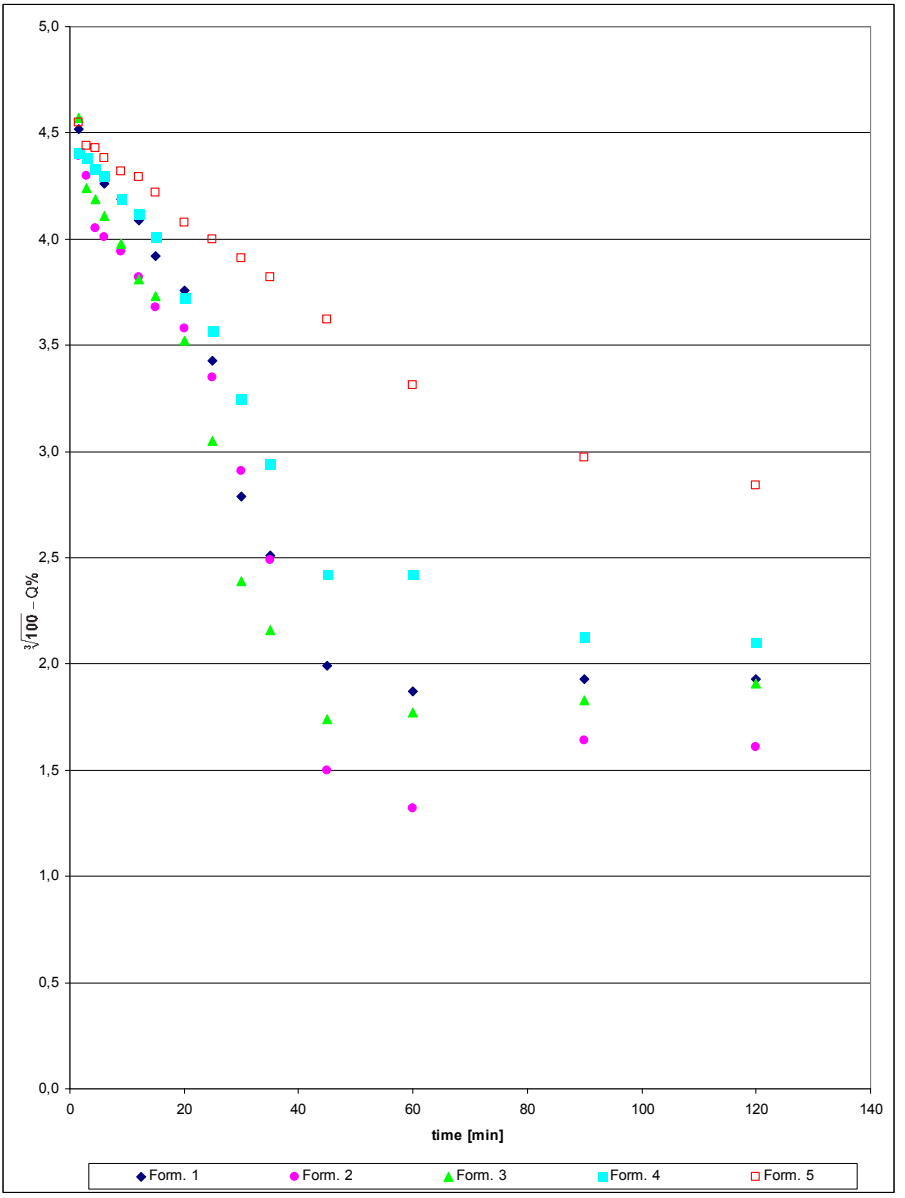

Figure 3.

Relationship between $\sqrt[3]{100} - Q\%$ with time ($\sqrt{t}$) for Hixon-Crowell diffusion model for water as medium

As can be seen in table 5, approximation equations of high correlation coefficient $r^2 \geq 0.9000$ describing the rate of dissolution of phytochemicals in water, that the equation $\log Q(\%) = a + b \cdot \log x$ for formulations F-1÷F-5 are characterized by

the highest correlation coefficient, irrespective of the mathematical model. This essentially applies to the model of zero and first order kinetics and to Higuchi model.

Also, in the model acceptor fluid (0.1 mol aqueous solution of HCl), the dissolution of phytochemicals after tablet disintegration against time (t, min), at a high correlation coefficient $r^2 \geq 0.9500$, is described as follows: $\log Q(\%) = a + b \cdot \log x$. This equation applies to all formulations F-1÷F-5. Surprisingly, high correlation coefficient values were found to be associated with the Hixon-Crowell model in the formulations F-2, F-4, F-5 for zero and first-order kinetics (tab. 5 and 6).

Table 5.

Correlation equations describing kinetics of solubility of phytochemicals contained in a tablet with *Ext. Taraxaci e radix cum herba aqu. siccum* in water at $p=0.05$

Medium formulation	Function type	Equation type	Correlation coefficients r	Slope coefficients of equations	
				a	b
Water F–1; n=15	Q=f(t)	y=a+b·log x	0.9502	–16.200	56.5002
		log y=a+b·log x	0.9720	0.8674	0.6123
	Q=f($\sqrt{t}$)	y=a+b·x	0.9247	1.5529	10.5647
		log y=a+b·log x	0.9722	0.8684	1.2232
	$\sqrt[3]{100}$–Q=f(t)	y=a+b·x	0.86646	4.1508	$-2.5970 \cdot 10^{-2}$
		log y=a+b·log x	0.9192	5.4619	–1.7332
Water F–2; n=15	Q=f(t)	y=a+b·log x	0.9633	–2.9299	51.0202
		log y=a+b·log x	0.9737	1.1632	0.4498
	Q=f($\sqrt{t}$)	y=a+b·x	0.9326	13.3585	9.4864
		log y=a+b·log x	0.9741	1.1639	0.8986
	$\sqrt[3]{100}$–Q=f(t)	y=a+b·x	0.8646	3.9862	$-2.7730 \cdot 10^{-2}$
		log y=a+b·log x	0.9066	5.3555	–1.8260
Water F–3; n=15	Q=f(t)	y=a+b·log x	0.9629	–16.200	56.5002
		log y=a+b·1/x	0.9673	0.8674	0.6123
	Q=f($\sqrt{t}$)	log y=a+b·log x	0.7848	1.5529	10.5647
		log y=a+b·1/x	0.8265	0.8684	1.2232
	$\sqrt[3]{100}$–Q=f(t)	y=a+b·log x	0.9322	4.1508	$-2.5970 \cdot 10^{-2}$
		log y=a+b·log x	0.9071	5.4619	–1.7332
Water F–4; n=15	Q=f(t)	y=a+b·log x	0.9493	–2.9299	51.0202
		log y=a+b·log x	0.9748	1.1632	0.4498
	Q=f($\sqrt{t}$)	y=a+b·x	0.9471	13.3585	9.4864
		log y=a+b·log x	0.9748	1.1639	0.8986
	$\sqrt[3]{100}$–Q=f(t)	y=a+b·x	0.9265	3.9862	$-2.7730 \cdot 10^{-2}$
		log y=a+b·log x	0.9405	5.3555	–1.8260
Water F–5; n=15	Q=f(t)	y=a+b·log x	0.9506	–2.9299	51.0202
		log y=a+b·log x	0.99903	1.1632	0.4498
	Q=f($\sqrt{t}$)	y=a+b·x	0.9922	13.3585	9.4864
		log y=a+b·log x	0.9902	1.1639	0.8986
	$\sqrt[3]{100}$–Q=f(t)	y=a+b·x	0.9791	3.9862	$-2.7730 \cdot 10^{-2}$
		log y=a+b·log x	0.9931	5.3555	–1.8260

Table 6.

Correlation equation describing kinetics of the solubility of phytochemicals contained in a tablet with *Ext. Taraxaci e radix cum herba aqu. siccum* in 0.1 mol HCl at $p=0.05$

Medium formulation	Function type	Equation type	Correlation coefficients r	Slope coefficients of equations	
				a	b
0.1 mol HCl F–1; n=15	Q=f(t)	y=a+b·x	0.9201	14.5241	0.7815
		log y=a+b·log x	0.9868	0.5036	0.7595
	Q=f($\sqrt{t}$)	log y=a+b·x	0.9769	–9.7993	10.0092
		log y=a+b·log x	0.9870	0.5049	1.5174
	$\sqrt[3]{100}$–Q=f(t)	y=a+b·log x	0.8858	–6.7467	0.8386
		log y=a+b·log x	0.8469	0.4492	$1.3320\cdot10^{-2}$
0.1 mol HCl F–2; n=15	Q=f(t)	y=a+b·x	0.9292	12.7263	0.7596
		log y=a+b·log x	0.9851	0.5356	0.7161
	Q=f($\sqrt{t}$)	y=a+b·x	0.9739	–10.3349	9.6074
		log y=a+b·log x	0.9858	0.5314	1.4376
	$\sqrt[3]{100}$–Q=f(t)	y=a+b·x	0.9546	4.4962	$-1.9901\cdot10^{-2}$
		1/y=a+b·log x	0.9694	0.2147	$1.7199\cdot10^{-3}$
0.1 mol HC F–3; n=15	Q=f(t)	y=a+b·log x	0.9496	10.1456	0.7562
		log y=a+b·log x	0.9901	0.4035	0.7796
	Q=f($\sqrt{t}$)	y=a+b·x	0.9856	–11.9517	9.4192
		log y=a+b·log x	0.9935	0.4341	1.5234
	$\sqrt[3]{100}$–Q=f(t)	1/y=a+b·x	0.5726	0.2013	$1.3985\cdot10^{-3}$
0.1 mol HCl F–4; n=15	Q=f(t)	y=a+b·log x	0.9618	–11.9656	45.8479
		log y=a+b·log x	0.9902	0.8910	0.5447
	Q=f($\sqrt{t}$)	y=a+b·x	0.9688	0.9648	8.8735
		log y=a+b·log x	0.9903	0.8919	1.0882
	$\sqrt[3]{100}$–Q=f(t)	y=a+b·x	0.9355	4.2907	$-1.8602\cdot10^{-2}$
		1/y=a+b·x	0.9638	0.2275	$1.6736\cdot10^{-3}$
0.1 mol HCl F–5; n=15	Q=f(t)	y=a+b·x	0.9698	11.8675	0.6445
		log y=a+b·log x	0.9963	0.6301	0.6212
	Q=f($\sqrt{t}$)	y=a+b·x	0.9938	–6.7799	7.9667
		log y=a+b·x	0.9964	0.6312	1.2409
	$\sqrt[3]{100}$–Q=f(t)	y=a+b·x	0.9905	4.4994	$1.5406\cdot10^{-2}$
		log y=a+b·x	0.9952	0.6573	$-1.8342\cdot10^{-3}$
		1/y=a+b·x	0.9968	0.2171	$1.8342\cdot10^{-3}$

Changes in the pH(a_{H+}) and osmolarity of the phosphate buffer significantly affected the solubility of the phytochemicals and their adsorption isotherm for the Prosolv and Vivapur 200 excipients. The presence of glycosidic-bond hydrolysis mechanisms in phosphate buffer, along with a real absence of micellar and hydrotropic solubilization, also affected the real solubility of the phytochemicals, which was found to be not higher than Q(%)≈87.0%. According to the approximation equations given in table 7, the dissolution of phytochemicals in the zero

and first-order kinetic and Higuchi models can be described by the equation log Q(%)=a+b·log x at high values of the correlation coefficient $r^2 \geq 0.9600$.

Table 7.

Correlation equation describing kinetics of solubility of phytochemicals contained in a tablet with *Ext. Taraxaci e radix cum herba aqu. siccum* in a phosphate buffer of pH=6.88 at $p=0.05$

Medium Formulation	Function type	Equation type	Correlation coefficients r	Slope coefficients of equations	
				a	b
Phosphate buffer of pH=6.88 F–1; n=15	Q=f(t)	y=a+b·log x	0.9541	–13.4805	49.1215
		log y=a+b·log x	0.9738	0.8569	0.5815
	Q=f($\sqrt{t}$)	y=a+b·log x	0.9539	–13.3836	98.1135
		log y=a+b·log x	0.9738	0.8580	1.1617
	$\sqrt[3]{100}$ –Q=f(t)	y=a+b·log x	0.9362	5.1695	–1.2588
		y=a+b·x	0.8622	4.2044	$1.8460 \cdot 10^{-2}$
Phosphate buffer of pH=6.88 F–2; n=15	Q=f(t)	y=a+b·log x	0.9528	1.9737	43.0906
		log y=a+b·log x	0.9716	1.1659	0.4199
	Q=f($\sqrt{t}$)	y=a+b·log x	0.9645	–0.6402	91.0277
		log y=a+b·log x	0.9679	1.1428	0.8806
	$\sqrt[3]{100}$ –Q=f(t)	y=a+b·x	0.9522	4.9616	–1.2662
		1/y=a+b·log x	0.9417	0.7243	–0.1642
Phosphate buffer of pH=6,88 F–3; n=15	Q=f(t)	y=a+b·log x	0.9599	–16.8767	49.3521
		log y=a+b·log x	0.9808	0.7288	0.6488
	Q=f($\sqrt{t}$)	log y=a+b·1/x	0.9410	1.9782	–1.6046
		y=a+b·1/x	0.7942	73.4408	–105.2497
	$\sqrt[3]{100}$ –Q=f(t)	log y=a+b·x	0.9453	0.6423	$-2.6742 \cdot 10^{-3}$
		log y=a+b·x	0.9547	0.2235	$1.9049 \cdot 10^{-3}$
Phosphate buffer of pH=6.88 F–1; n=15	Q=f(t)	y=a+b·log x	0.9668	–11.3322	50.3408
		log y=a+b·log x	0.9796	0.9409	0.5501
	Q=f($\sqrt{t}$)	y=a+b·log x	0.9667	–11.2338	100.5497
		log y=a+b·log x	0.9797	0.9418	1.0988
	$\sqrt[3]{100}$ –Q=f(t)	log y=a+b·x	0.9131	0.6229	$-2.8306 \cdot 10^{-3}$
		y=a+b·log x	0.9426	5.2067	1.3801
Phosphate buffer of pH=6.88 F–2; n=15	Q=f(t)	y=a+b·x	0.9662	11.0097	0.6692
		log y=a+b·log x	0.9786	0.4522	0.7399
	Q=f($\sqrt{t}$)	y=a+b·x	0.9948	–8.9191	8.3633
		log y=a+b·log x	0.9825	0.4183	1.5223
	$\sqrt[3]{100}$ –Q=f(t)	y=a+b·x	0.9880	4.5161	$-1.6159 \cdot 10^{-2}$
		1/y=a+b·log x	0.9932	0.6592	$-1.9357 \cdot 10^{-3}$
		1/y= a+b·x	0.9944	0.2157	$1.2501 \cdot 10^{-3}$

Interestingly, the approximation equations for the formulations F-3 and F-5 differ significantly for the Hixon-Crowell model, which indicates that effective solubility has a regressive function. This is reflected in the following equations, with a high correlation coefficient $r^2 \geq 0.9500$: y=a+b·x, log y=a+b·x i 1/y= a+b·x.

CONCLUSIONS

1. Silicified (SiO_2 film) microcrystalline Prosolv-type cellulose, Vivapur 200 with homogeneous granulometric composition and Emdex are compatible with the structure of *Ext. Taraxaci e radix cum folium aqu. siccum*. They can therefore be used to manufacture a model of a solid oral form of a drug with desired morphological parameters. The disintegration time complies with pharmacopoeial requirements (tab. 1), but is slightly prolonged in 0.1 mol HCl and phosphate buffer at pH(a_{H+}) 6.88.
2. While the dissolution process is comparable between formulations F-1 and F-4, it is considerably reduced (inhibited) in the presence of Emdex (tab. 2-4). In the absence of micellar solubilization, the rate of the dissolution of phytochemicals is determined by physico-chemically complex hydrotropic solubilization and, more importantly, the number of glycosidic bonds between sugar alcohols and the lipophilic aglycones of the phytochemicals. While the composition of the model tablet uses only a single excipient, thus allowing direct compression and bestowing significant sorption properties, the Q(%) coefficient varies significantly in 0.1 mol HCl and phosphate buffer at pH(a_{H}^{+}) 6.88.
3. The dissolution of the phytochemicals after the disintegration of the model tablet is represented in a mathematical diffusion model (Higuchi model, Krosmeyer-Peppas model, and Hixon-Crowell model) based on correlation equations given in tables 5-7 ($p=0.05$). Irrespective of the analyzed mathematical model, this type of process is most frequently described by equations of the following type: $\log y=a+b\cdot\log x$ (the logarithmic form of the exponential equation $Q(\%)=k\cdot t^n$ in the Krosmeyer-Peppas model), assuming $\sim r^2\geq 0.900$ as a criterion of application reliability. Surprisingly, formulations F-4 and F-5 demonstrated high correlation coefficients ($p=0.05$) in aqueous medium, obtained by equations of the types $y=a+b\cdot x$ and $1/y=a+b\cdot x$ for the Hixon-Crowell model.
4. In the 0.1 mol HCl (change of osmolarity and pH(a_{H}^{+})=1.86) or in phosphate buffer (pH=6.88), the process of dissolution at high correlation coefficients $r^2\geq 0.950$ was also described by $\log y=a+b\cdot\log x$ (at approximately $p=0.05$). Surprisingly, for the Hixon-Crowell regression model in the presence of excipients, for formulations F-3 and F-5 in phosphate buffer, the dissolution rate was described by the correlation equations $y=a-b\cdot x$, $\log y=a-b\cdot x$ and $1/y=a-b\cdot x$ at $r^2\geq 0.945$.
5. In this study, the rate of dissolution was found to depend on the pH(a_{H}^{+}) of the pharmacopoeial acceptor liquid medium and on the adsorptive capacity of the excipients (Freundlich adsorption isotherm). Importantly, the process of dissolution examined herein is most comprehensively described by the Krosmeyer-Peppas equation $y = k\cdot t^n$, (its application form being $\log Q(\%) = a + b \bullet t$, where $a = \log k$). An interesting aspect of *Taraxaci e radix cum folium radix aqu. siccum* is its observed partial adsorption on the surface of

silicified microcrystalline cellulose (Prosolv), which decreases the value of Q(%) (tab. 3, 4). This also allows the equations underpinning the diffusion models (Fick's equation), particularly the Hixon-Crowell model, to describe the rate of dissolution at high values of the correlation coefficient r^2.

Conflict of interest: Authors declare no conflict of interest.

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FORMULACJA I PROFIL DOSTĘPNOŚCI FARMACEUTYCZNEJ Z MODELOWEJ STAŁEJ DOUSTNEJ POSTACI LEKU FITOZWIĄZKÓW ZAWARTYCH W SUCHYM MIANOWANYM EKSTRAKCIE Z MNISZKA LEKARSKIEGO (*TARAXACUM OFFICINALE*, COLL.)

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S t r e s z c z e n i e

Wstęp: Mniszek lekarski (*Taraxacum officinale* coll.) zwany też mniszkiem pospolitym, rośnie dziko w całej Europie, Azji i obu Amerykach. Jest wieloletnią rośliną z rodziny astro-

watych (*Asteraceae*). Wykazuje wszechstronne właściwości lecznicze. Surowcem zielarskim jest cała roślina: kwiaty, korzenie i liście. **Cel:** Celem pracy było wytworzenie przez bezpośrednie tabletkowanie suchego mianowanego ekstraktu z mniszka lekarskiego z użyciem wybranych substancji pomocniczych modelowych tabletek o farmakopealnym czasie rozpadu. **Metody:** Tabletki otrzymano metodą bezpośredniego tabletkowania przy użyciu tabletkarki uderzeniowej firmy Erweka. Zbadano parametry morfologiczne, tj. twardość, ścieralność, czas rozpadu w farmakopealnych płynach biorczych (akceptorowych) za pomocą urządzeń firmy Erweka, a także wyliczono ich powierzchnię rzeczywistą. Przeprowadzono również badanie szybkości procesu rozpuszczania się fitozwiązków w obecności substancji pomocniczych z modelowych tabletek w środowisku farmakopealnych płynów biorczych w aparacie firmy Erweka metodą koszyczkową w objętości płynu akceptorowego V=1,0 dm^3. Wykonano oznaczenia spektrofotometryczne. **Wyniki:** Z uzyskanych rezultatów badań morfologicznych modelowych tabletek zawierających *Ext. Taraxaci e radix cum herba aqu. siccum* wynika, że charakteryzują się one porównywalną powierzchnią rzeczywistą i ścieralnością przy zróżnicowanej twardości, która jest wynikiem zastosowanych substancji pomocniczych. Znajduje to odzwierciedlenie w efektywnym czasie rozpadu w modelowych płynach biorczych, zgodnym z wymogami farmakopealnymi. **Wnioski:** Zastosowane substancje pomocnicze umożliwiły otrzymanie modelowych tabletek metodą bezpośredniego tabletkowania, zawierających suchy mianowany wyciąg z mniszka lekarskiego. Z uzyskanych rezultatów badań wynika, że mikrokrystaliczna celuloza typu Prosolv oraz Vivapur 200 i Emdex są kompatybilne ze strukturą wyciągu z mniszka lekarskiego. Umożliwiają one wytworzenie modelowej stałej doustnej postaci leku o oczekiwanych parametrach morfologicznych i efektywnym, zgodnym z wymogami farmakopealnymi czasem rozpadu.

Słowa kluczowe: *Taraxacum officinale*, tabletkowanie bezpośrednie, solubilizacja, rozpuszczalność fitozwiązków, dostępność farmaceutyczna.