® Postepy Hig Med Dosw (online), 2013; 67: 1154-1165
e-ISSN 1732-2693

www.phmd.pl
Original Article

Received: 2012.12.12
Accepted: 2013.07.22
Published: 2013.11.28

Taxon analysis of seed plants used in studies of blood platelet function*

Analiza taksonów roślin nasiennych wykorzystywanych w badaniach płytek krwi

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Magdalena Boncler[A, B, C, D, E, F], **Cezary Watała** [C, E, G]

Department of Haemostatic Disorders, Medical University of Lodz, Lodz, Poland

Summary

The characterization of isolated polyphenolic compounds present in the diet – especially in the context of their therapeutic effect (for instance their antiplatelet activity) – is often based on the generally accepted flavonoid classification. In the case of plant extracts it usually refers to common names of plants rather than scientific botanical nomenclature. Hence, it is often difficult to even roughly estimate how many and which plant taxa exhibit biological activity towards the modulation of blood platelet activity. In this paper, based on a review of literature from the last 50 years (1962-2011), we developed a list of seed plants (*Spermatophyta*) taxa investigated in studies on blood platelets. We used the PubMed database, as well as the database of species' names - Taxonomy, in order to gather information about the investigated taxa. The review of the literature was made with the use of advanced options, on the basis of keywords (or combinations of keywords) and selected journals. Record search strategies were evaluated on the basis of the sensitivity of search (number of papers meeting the criteria of search strategy) and the specificity of search (number of papers containing in their title and/or abstract information on taxa used in blood platelet research). The publications were considered specific if they reported either Latin or common names of plants (or both). The main search strategy was characterised by high sensitivity, but low specificity. The basis for plant taxonomic specification was the list of 1080 articles, published in 434 journals. The list of taxa used in blood platelet studies covered 98 genera belonging to 47 families of seed plants. The richest in genera, and also in species, appeared to be the families *Asteraceae*, *Fabaceae*, and *Rosaceae*, the most abundant in species all over the world. This study may be a starting point for the selection of plant species to be used for biomedical research and – at the same time – may help in the search for an effective strategy of literature tracking concerning flavonoids and blood platelets.

Key words: **flavonoids • blood platelets • taxon • polyphenolic compounds**

Full-text PDF: http://www.phmd.pl/fulltxt.php?ICID=1077854

Word count: 4120
Tables: 4
Figures: 2
References: 125

Author's address: Dr Magdalena Boncler, Department of Haemostatic Disorders. Chair of Laboratory Diagnostics, Medical University of Lodz, Central Veteran's Hospital, 113 Zeromski Street, 90-549 Lodz; email: magdalena.boncler@umed.lodz.pl

*This work was supported by the project "FLAWOPIRYNA", UDA-POIG.01.03.01-10-129/08-00, financed by the European Regional Development Fund within the framework of the Innovative Economy Programme 2007-2013.

Introduction

Polyphenolic compounds of plant origin are very important components of the human diet due to their antioxidant activity, their ability to scavenge free radicals and their potential of reducing tissue damage caused by oxidative stress, which accompanies, to a greater or lesser extent, all chronic diseases. A large group of polyphenolic compounds present in the diet is constituted by flavonoids and, therefore, it is flavonoids that are most often the subjects of scientific research [72]. It has been observed that the consumption of fruits and vegetables (a diet rich in polyphenols) prevents the development of cardiovascular diseases, such as coronary heart disease or stroke [17,37,88]. The cardioprotective properties of polyphenols are related to, *inter alia*, the antiplatelet activity of flavonoids, confirmed in numerous publications. Investigations on the regulation of blood platelet function by polyphenolic compounds involve either reports concerning pure polyphenols with known chemical structure (e.g. quercetin, an inhibitor of tyrosine kinases) [116] or multi-component plant extracts [121]. The nomenclature of the investigated polyphenolic compounds refers either to the generally accepted classification of flavonoids (in the case of isolated compounds) or to the colloquial names of plants (in the case of multi-component extracts). The scientific botanical nomenclature is seldom used or mentioned. Doing so certainly makes a scientific text easier; however, at the same time, it makes the synthesis of study of polyphenols as natural inhibitors of blood platelets much more difficult to comprehend in the botanical context. In order to determine the antiplatelet activity of extracts from plants, which are a source of polyphenolic compounds, we aimed to develop of a list of taxa of seed plants (Spermatophyta) used worldwide in platelet studies. To achieve this objective, different literature search strategies were employed using PubMed, which were also assessed for their sensitivity and specificity. Therefore, this study may serve as a starting point in the selection of plant species intended for biomedical research and may provide a direction in the effective assessment of the literature on polyphenolic compounds as modulators of blood platelet function.

Materials and methods

The literature search was conducted from February to March 2012, using the PubMed database of scientific literature. Plants described in the publications were analysed with respect to their taxonomy, employing a database of species names (Taxonomy). The study covered the literature published in the years 1962–2011. All queries were built with advanced search options. The strategy of literature review was adapted to the aim of our research, which was a taxonomical analysis of vascular plants (*Euphyllophyta*), belonging to the seed plants (*Spermatophyta*) and excluding spore plants (*Moniliformopses*), that were used in studies dedicated to blood platelets (Fig. 1).

The research was divided into stages. The first stage began with the selection of keywords, allowing us to collect literature in PubMed in a satisfactory number, regardless of the publication date. For this purpose, the following search options were included:

Strategy 1 (#1): flavonoids AND platelet*

Strategy 2 (#2): polyphenols AND platelet*

Strategy 3 (#3): polyphenolic compounds AND platelet*

First, for an optimal search option, the number of publications indexed by PubMed in consecutive years was compared, starting from the year of the oldest publication appeared until 2011. The aim of this stage was to determine the time of the intense increase in the number of publications on the biological activity of polyphenolic compounds in the context of blood platelet research. The allocation of papers to the groups of publications containing (specific) or not containing (nonspecific) the required information on plant taxa used in blood platelet research was conducted in the second stage. Information on plant taxa used in blood platelet research was gained solely from the titles and/or abstracts of publications. During the process of gathering information on plant taxa we prepared a list of journals, in which the analysed papers appeared most frequently. This list was used to verify the correctness of the chosen strategy, amongst options #1-#3, by assuming the following search options #4-#6:

Strategy 4 (#4): flavonoids AND platelet* AND journal

Strategy 5 (#5): polyphenols (NOT flavonoids) AND platelet* AND journal

Strategy 6 (#6): (polyphenols OR flavonoids) AND platelet* AND journal

The third stage was to draw up a list of taxa (genera/species and families) used in the studies on platelets. In order to avoid omitting taxa relevant to platelet research, the units of plants occurring in publications (title and/or abstract), which did not refer to studies of blood platelets, were additionally verified with strategy #7:

Strategy 7 (#7): (genus name) AND platelet*

In addition to the list of taxa, a ranking of the families richest in genera/species used in blood platelet research was compiled.

Analysis of results

The basis of this study was the publications indexed by the PubMed database (http://www.ncbi.nlm.nih.gov/pubmed/). In the compilation of the list of taxa associated with plants used in blood platelet studies, the Taxonomy database (http://www.ncbi.nlm.nih.gov/

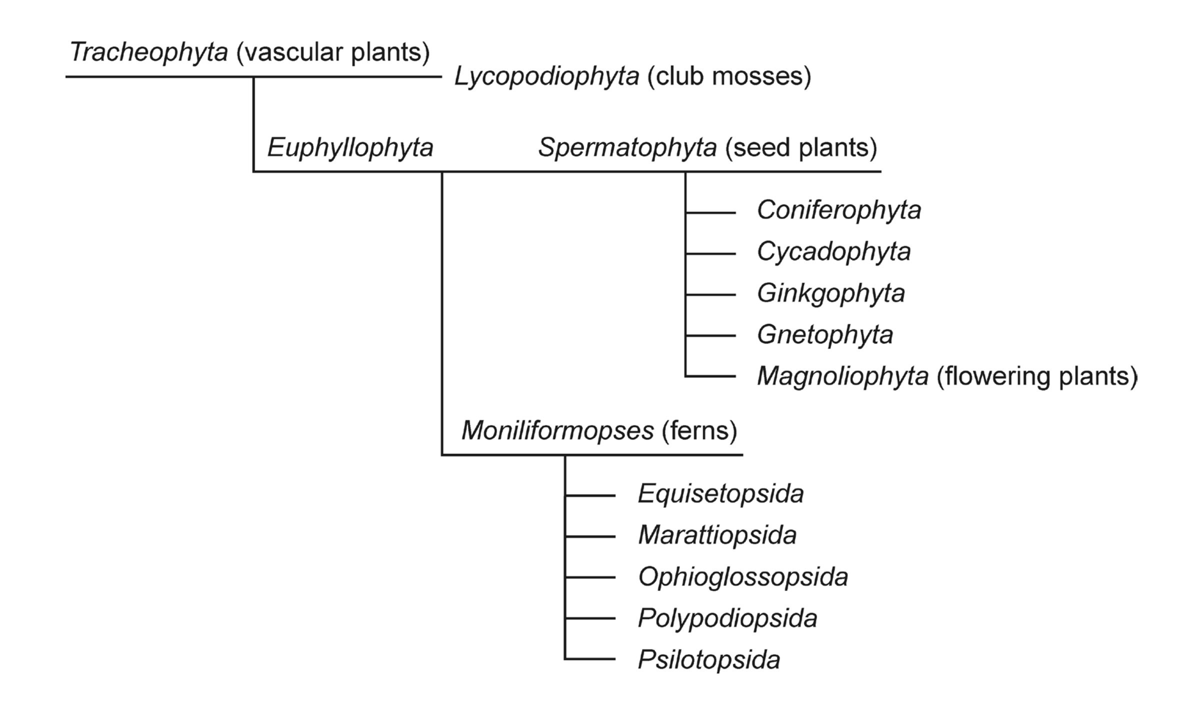

Fig. 1. Cladogram showing the phylogenetic relationships among vascular plants

taxonomy) was employed. Search strategies were compared in terms of sensitivity, determined by the number of studies meeting the criteria of the search strategy. The analysis of publications was carried out in terms of specificity of the search (calculated as the number of articles containing in their title and/or abstract the information on taxa used in blood platelet research). The publications giving the names of taxa according to botanical nomenclature or articles containing common names of plants were regarded as specific. The employed measures of central tendency and diversity were the median and interquartile range (25% to 75%). Depending on the characteristics of distribution, for testing the differences between the groups, we employed Student's *t* test for paired data or Wilcoxon's test.

Results

Stage 1

For the entire searched time range (i.e. without specifying the time range), the number of records found in PubMed for strategies #1-#3 varied and amounted to: 1081 (#1), 151 (#2), 45 (#3).

The MeSH database had been primarily used in the study to find MeSH terms for a PubMed search. When we entered the terms "flavonoids", or "polyphenols" we did not find any other relevant MeSH concepts, whereas by entering the term "platelet" we succeeded in finding over 140 MeSH terms. From our point of view, in terms of taxon analysis, the most relevant results were: blood platelets, platelet function, platelet activation and platelet aggregation; however, none of the chosen MeSH terms used for a literature search in conjunction with the term "flavonoids" resulted in finding a larger number of records than the number of records attributed to strategy #1. Thus, finally, for the assessment of search specificity (i.e. for the assessment of the number of publications indexed by the PubMed database according to the topic, as well as for the selection of publications containing information on the taxa of plants used in blood platelet studies), strategy #1 was employed. When using this strategy, we noted that the oldest record returned by PubMed was from 1962, while the most recent was from 2012. Therefore, we decided to analyse the data originating from the literature published in the years 1962-2011, i.e. we included 1080 papers in the analysis. Until 1985, the number of papers indexed by PubMed did not exceed 10 annually. A sharp increase in the number of indexed papers came in the late 1990s, i.e. from 1995 on, since more than 30 papers annually appeared in the database. The average number of publications in the years 1995-2011 was 59 (48-61) [Me (LQ-UQ)]. Figure 2 shows the number of papers indexed by PubMed by decade in the period 1962-2011. What follows is that interest in the subject of antiplatelet function of polyphenolic compounds gradually increased in each decade, but the greatest increase in the number of records on this topic occurred in the last decade of the last century (Fig. 2). In contrast to this, beginning from the second decade, i.e. after 1980, the number of all journals indexed in PubMed decreased (Fig. 2). Interestingly, since 2002, the summed number of records returned by PubMed in the subsequent years of the period 2002-2011 was higher by 52 records than the number of records searched in the database for the period of 2002-2011 (538 records).

Stage 2

Taking into account the titles and abstracts of publications obtained for strategy #1, we assigned a review of seed plant taxa that were used in studies on blood platelets. Out of 1080 records, 683 publication titles and/or abstracts did not contain the systematic names of families, genera or species of plants that served to provide the investigated polyphenolic compounds. Thus, only 397 items out of the initial pool of 1080 records were utilised to compile the taxonomical list of plants used in these studies. Excluded were also two duplicates and one publication on the *Pteris* genus, which, according to the contemporary systematics of plants, belongs to the group of spore plants *Moniliformopses*, which was excluded from this study.

Publications from the period of 1962-1984 (n=43) appeared to be irrelevant to the elaboration of the taxonomical list, because neither the titles nor the abstracts (if present) of these records contained any valid information on taxa. The first work encountered providing the taxonomical plant name was from 1985. In the following years, the number of such publications increased; after 1997 this figure exceeded 10 per year, and after 2001 it was greater than 20 papers per calendar year. Most records referring to blood platelets and containing information on the taxonomy of the used plants were published in 2008 (42 publications).

In addition to the selection of articles on the basis of information on taxa, we performed a review of the journals, in which publications found with strategy #1 appeared. The analysis revealed that 1080 articles returned by PubMed appeared in as many as 434 journals, (on average, 2.5 publications per journal). For comparison, in the period of the last decade (2002-2011), 538 articles were published in 269 journals (on average, 2 articles per journal). The share of individual journals, in the pool of records determined by strategy #1 is shown in Table 1. The first three positions were occupied by *The Journal of Biological Chemistry*, *Thrombosis Research* and *Biochemical Pharmacology*. Making use of this ranking (i.e. the 10 journals, in which publications on flavonoids and platelets appeared most often), we verified the desirability of pursuing strategy #1 by comparing the number of records returned to strategies #4-#6. The average number of records returned by PubMed with strategy #4 was significantly higher than the number of records obtained with strategy #5 (Me; LQ-UQ: 17.5; 16-24 papers vs. 0; 0-1 papers; p=0.002), but it did not differ from the number of publications collected with strategy #6 (18.5; 16-24 records). The partial data for this comparison are summarised in Table 2.

Stage 3

On the basis of the review of literature recorded in the PubMed database in the period of 1962-2011 and found

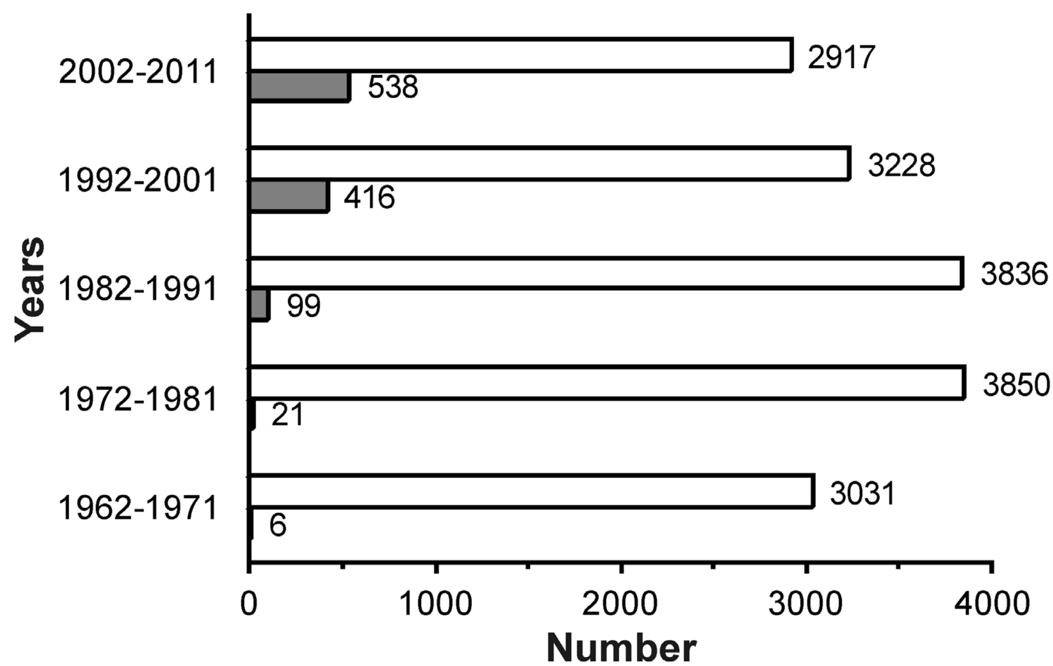

Fig. 2. The number of records returned by PubMed for strategy #1 (black bars) and the number of all journals referenced in PubMed (white bars) in consecutive decades in the period 1962-2011

Table 1. Proportion of journals publishing papers on flavonoids and blood platelets

Journal name	No. of articles (n)	%
The Journal of Biological Chemistry	35	3.2
Thrombosis Research	25	2.3
Biochemical Pharmacology	24	2.2
European Journal of Pharmacology	24	2.2
Biochemical and Biophysical Research Communications	18	1.7
Biological and Pharmaceutical Bulletin	17	1.6
Platelets	17	1.6
Planta Medica	16	1.5
Journal of Natural Products	15	1.4
Journal of Nutrition	14	1.3
Prostaglandins, Leukotrienes and Essential Fatty Acids	14	1.3
Journal of Cardiovascular Pharmacology	13	1.2
Zhongguo Zhong Yao Za Zhi	13	1.2
Journal of Agricultural and Food Chemistry	12	1.1
Zhongguo Yao Li Xue Bao	12	1.1
American Journal of Physiology	11	1.0
Biochemical Journal	11	1.0
Circulation	11	1.0
FEBS Letters	11	1.0
Journal of Thrombosis and Haemostasis	11	1.0
British Journal of Pharmacology	10	0.9
remaining journals (413)	<10 (746)	69.07
Total	1080	100

Table 2. Comparison of search sensitivity (number of papers meeting the criteria of the search strategy) for strategies #4-#6

Journal name	Strategy #4	Strategy #5	Strategy #6
	No. of records (n)		
The Journal of Biological Chemistry	35	0	35
Thrombosis Research	25	4	29
Biochemical Pharmacology	24	0	24
European Journal of Pharmacology	24	0	24
Biochemical and Biophysical Research Communications	18	1	19
Biological and Pharmaceutical Bulletin	17	0	17
Platelets	17	1	18
Planta Medica	16	0	16
Journal of Natural Products	15	0	15
Journal of Nutrition	14	1	15
Total	205	7	212

by strategy #1, we developed our list of taxa. Many papers contained in their content (title and/or abstract) common names, such as apple, berry, olive, etc. Not to miss publications of this kind, and yet to avoid a mistake in determining the species names, the taxonomic list contains the names of plant genera and their affiliations to families, assigned according to contemporary plant taxonomy. In the pool of 394 publications containing the information on taxa, about 25% of the papers did not relate directly to blood platelet research, but to other cell types, such as endothelial cells, smooth muscle cells, leukocytes, cancer cells, hepatocytes, etc. Of these papers we distinguished publications referring to 18 plant genera, the significance of which in blood platelet research was verified again using strategy #7 (see M&M). If for strategy #7 the PubMed search database provided a paper concerning a biological activity of a given genus in relation to blood platelets, this genus was placed on the taxa list. Otherwise, the taxon was not taken into consideration. On this basis, the taxa list was expanded by nine genera, while the remaining nine genera were excluded. The group of eliminated genera consisted of: *Bauhinia sp., Millettia sp., Gongronema sp., Sarcophyte sp., Machilus sp., Galphimia sp., Hibiscus sp., Cudrania sp., and Apium sp*.

Finally, the taxonomical list contained 98 genera belonging to 45 families and an additional two families without specified genera (*Saururaceae* and *Orchidaceae*) (Table 3). The most abundant in genera, as well as in species, were the families *Asteraceae* (19.4%), *Fabaceae* (15.3%) and *Rosaceae* (6.1%). The share of individual families in the pool of the presented taxa is shown in Table 4.

Discussion

Polyphenolic compounds, integral components of the diet, constitute a widespread and probably the most numerous group of chemical compounds occurring in higher plants. The cardioprotective effects of polyphenolic compounds have been widely reported in both in *in vivo* and *in vitro* studies. To a large extent, these effects are related to the antiplatelet activity of polyphenols. In a number of publications, particularly in review papers, the characteristics of known dietary polyphenolic compounds with antiplatelet activities is based on the accepted classification of flavonoids and, in the case of plant extracts, it often refers merely to the common names of plants, without any details on the botanical nomenclature. Therefore, the primary objective of this study was to establish a list of taxa of the seed plants used in blood platelet research. To the best of our knowledge, this is the first study investigating this topic. For the purpose

Table 3. List of taxa used in blood platelet research

Genus	Family	References
Abelmoschus sp.	*Malvaceae*	[39]
Abrus sp.	*Fabaceae*	[61]
Acalypha sp.	*Euphorbiaceae*	[47]
Achillea sp.	*Asteraceae*	[96]
Actinidia sp.	*Actinidiaceae*	[104]
Actinostemma sp.	*Cucurbitaceae*	[54]
Allium sp.	*Amaryllidaceae*	[6]
Alpinia sp.	*Zingiberaceae*	[50]
Anadenanthera sp.	*Fabaceae*	[40]
Andrographis sp.	*Acanthaceae*	[117]
Angelica sp.	*Apiaceae*	[33]
Annona sp.	*Annonaceae*	[9]
Arnica sp.	*Asteraceae*	[96]
Aronia sp.	*Rosaceae*	[87]
Artemisia sp.	*Asteraceae*	[84]
Artocarpus sp.	*Moraceae*	[49]
Astragalus sp.	*Fabaceae*	[118]
Brassica sp.	*Brassicaceae*	[78]
Broussonetia sp.	*Moraceae*	[56]
Bupleurum sp.	*Apiaceae*	[10]
Calamus sp.	*Arecaceae*	[8]
Camellia sp.	*Theaceae*	[10]
Capsicum sp.	*Solanaceae*	[111]
Carthamus sp.	*Asteraceae*	[66]
Chromolaena sp.	*Asteraceae*	[69]
Cichorium sp.	*Asteraceae*	[3]
Cistus sp.	*Cistaceae*	[30]
Citrus sp.	*Rutaceae*	[91]
Conyza sp.	*Asteraceae*	[96]
Crataegus sp.	*Rosaceae*	[112]
Curcuma sp.	*Zingiberaceae*	[50]
Dalbergia sp.	*Fabaceae*	[105]
Echinacea sp.	*Asteraceae*	[96]
Epimedium sp.	*Berberidaceae*	[13]
Erigeron sp.	*Asteraceae*	[90]
Erythrina sp.	*Fabaceae*	[83]
Euchresta sp.	*Fabaceae*	[70]
Ferulago sp.	*Apiaceae*	[30]
Ficus sp.	*Moraceae*	[36]
Flaveria sp.	*Asteraceae*	[38]
Fragaria sp.	*Rosaceae*	[74]
Gentiana sp.	*Gentianaceae*	[68]
Ginkgo sp.	*Ginkgoaceae*	[55]
Glycine sp.	*Fabaceae*	[59]
Glycyrrhiza sp.	*Fabaceae*	[106]
Helichrysum sp.	*Asteraceae*	[31]
Hippophae sp.	*Elaeagnaceae*	[15]
Humulus sp.	*Cannabaceae*	[85]
Ixora sp.	*Rubiaceae*	[65]
Kaempferia sp.	*Zingiberaceae*	[50]
Laurus sp.	*Lauraceae*	[4]
Lonicera sp.	*Caprifoliaceae*	[11]
Maackia sp.	*Fabaceae*	[92]
Malus sp.	*Rosaceae*	[103]
Matricaria sp.	*Asteraceae*	[96]
Melicope sp.	*Rutaceae*	[20]
Morus sp.	*Moraceae*	[56]
Muntingia sp.	*Muntingiaceae*	[14]
Myrica sp.	*Myricaceae*	[107]
Olea sp.	*Oleaceae*	[101]
Ononis sp.	*Fabaceae*	[1]
Oryza sp.	*Poaceae*	[119]
Perilla sp.	*Lamiaceae*	[46]
Petroselinum sp.	*Apiaceae*	[12]
Phyllanthus sp.	*Phyllanthaceae*	[45]
Pinus sp.	*Pinaceae*	[93]
Prunus sp.	*Rosaceae*	[120]
Psoralea sp.	*Fabaceae*	[110]
Pueraria sp.	*Fabaceae*	[18]
Punica sp.	*Lythraceae*	[73]
Rhaponticum sp.	*Asteraceae*	[57]
Rhododendron sp.	*Ericaceae*	[123]
Ribes sp.	*Grossulariaceae*	[74]
Rubus sp.	*Rosaceae*	[74]
Salix sp.	*Salicaceae*	[124]
Sambucus sp.	*Adoxaceae*	[21]
Santolina sp.	*Asteraceae*	[99]
Scutellaria sp.	*Lamiaceae*	[60]
Silybum sp.	*Asteraceae*	[94]
Solanum sp.	*Solanaceae*	[114]
Solidago sp.	*Asteraceae*	[96]
Sophora sp.	*Fabaceae*	[53]
Stachys sp.	*Lamiaceae*	[102]
Syzygium sp.	*Myrtaceae*	[22]
Tanacetum sp.	*Asteraceae*	[100]
Tephrosia sp.	*Fabaceae*	[51]
Theobroma sp.	*Malvaceae*	[77]

Trifolium sp.	*Fabaceae*	[58]
Tussilago sp.	*Asteraceae*	[44]
Typha sp.	*Typhaceae*	[125]
Urtica sp.	*Urticaceae*	[29]
Vaccinium sp.	*Ericaceae*	[75]
Varthemia sp.	*Asteraceae*	[2]
Viburnum sp.	*Adoxaceae*	[5]
Viscum sp.	*Viscaceae*	[97]
Vitis sp.	*Vitaceae*	[87]
Yucca sp.	*Asparagaceae*	[87]
Zingiber sp.	*Zingiberaceae*	[50]
n/a	*Saururaceae*	[71]
n/a	*Orchidaceae*	[67]

Table 4. Share of families richest in genera/species used in blood platelet studies

Family	No. of taxa (n)	%
Asteraceae	19	19.4
Fabaceae	15	15.3
Rosaceae	6	6.1
Apiaceae	4	4.1
Moraceae	4	4.1
Zingiberaceae	4	4.1
Lamiaceae	3	3.1
Adoxaceae	2	2.0
Ericaceae	2	2.0
Malvaceae	2	2.0
Rutaceae	2	2.0
Solanaceae	2	2.0
remaining	33	33.7
Total	47	100

of this analysis, we followed specific search strategies, which were further evaluated during the course of the study. The applied strategies proved to be helpful in the analysis of our results and allowed us to look critically at the effectiveness of the process of collecting literature concerning this subject.

The resulting outcome of the analysis was established in several stages. First of all, keywords were chosen to allow us to collect a satisfactory number of papers. Generally, we deliberately based our literature search on two terms (a broad search strategy) in order to find the highest possible number of specific papers without omitting any important articles in terms of taxonomic analysis. In our study only strategy #1 provided a satisfactory number of records. This may be related to the historically earliest appearance of the term "flavonoid" in the MeSH used for indexing PubMed citations. According to the MeSH database the term "flavonoids" was introduced in 1963, whereas the term "polyphenols" was only quite recently added to the MeSH database (2010). In turn, the phrase "polyphenolic compounds" has not been added so far to the thesaurus or MeSH.

The high sensitivity of strategy #1 in relation to the other ones (#2-#3) is evidence of the great interest in flavonoids as a group of polyphenolic compounds commonly occurring in the world of plants and present in the majority of foods or beverages originating from plants. First, we compared the number of publications indexed by PubMed in consecutive years and decades during the last 50 years. This allowed us to determine that the period of rapid growth of the number of publications on this topic occurred in the second half of the 1990s. This is most likely related to growing interest in the subject of the antiplatelet properties of polyphenolic compounds rather than to the number of journals referenced in PubMed at that time. Assuming that the time-dependent fluctuations in the number of journals referenced in PubMed containing the analysed reports are proportional to the time-dependent changes in the number of all journals indexed in PubMed, the chance of revealing a positive correlation between the number of collected articles and the number of journals indexed in PubMed and publishing these articles seems low (Fig. 2). It means that the interest in the role of flavonoids in platelet function is probably not affected by the number of journals indexed in PubMed in 1990s. This is even more likely considering that 1) the list of currently indexed journals differs from the list of previously indexed journals and 2) the total number of journals, in which the analysed articles have been published is as high as 434 titles. In the course of this analysis, we noted that the total number of records returned by PubMed for each calendar year during the period of 2002-2011 was not equal to the number of records returned by PubMed for the entire decade of 2002-2011. The reason for such an inconsistency was the occurrence of duplicates, which one can convince oneself of when saving the records in a clipboard; when doing so, we did not add records already present in it, thus eliminating duplicates. In the group of eliminated duplicates, we found publications described with two dates: the release date of publication in the journal and the date of issue in electronic form, available on the Internet; the years of issue of these publications in printed journals differed from the years of publication issue in their electronic forms. This is highly likely to occur when the release of an article in a journal falls at the beginning of the calendar year, and the date of issue of publication in the electronic form precedes the release in the printed form of a journal by several months. As a consequence, a publication released in a journal, e.g. in 2003, but available online in the preceding year, could be found twice when performing a search of the literature only for 2003 or only for 2002, but only once when searching for the range of 2002-2003.

A selection of papers found with strategy #1, conducted at stage 2, allowed us to determine how many publications provided in their titles or abstracts information on the taxa of plants used in cell research (blood platelets by default). Surprisingly, the number of publications forming the basis of the taxa list was 1.7-fold lower compared to the number of papers not containing any information on taxa in their titles or abstracts. There were several reasons for the questionable usefulness of almost 683 records in the present study. Most of all, the search strategy, although sensitive in terms of the number of papers found, was not specific enough. The use of a wild card in strategy #1 significantly increased the number of returned records, but at the same time, the initial pool contained publications not fully meeting the search criteria. A large proportion of the publications did not contain in their title and/or abstract information on the taxa and/or was not related to blood platelet research. Instead of taxa names, often the names of particular polyphenolic compounds of plant origin appeared, including rutin, apigenin, and luteolin. The most commonly reported flavonoids included genistein, quercetin and catechins. Given the fact that the mentioned compounds have been the subject of research for many years due to their interesting biological activities and therapeutic properties, as well as due to their availability and their sources of origin in nature, the lack of taxonomical names in these publications is understandable. Most studies involving genistein, an isoflavonoid naturally occurring in leguminous plants (*Fabaceae* family), have focused on the activity of genistein as an inhibitor of tyrosine kinases, as well as the anticancer, cardioprotective and hormonal activity of this polyphenolic compound [26,35]. Quercetin is a flavonoid commonly occurring in fruits and vegetables, as well as in seeds, nuts, flowers, leaves and bark. It is known to possess strong antioxidant and anti-inflammatory properties, which are related to the prevention and treatment of cardiovascular diseases and cancer [52,95]. Catechins, especially abundant in tea leaves, cocoa, apples and red wine, possess antioxidant, antibacterial, antiviral, anticancer, hypolipaemic, hypoglycaemic and hypotensive properties [41].

The low specificity of the adopted search strategy also resulted from the presence of articles containing the keyword "platelet", but often not having, besides the term itself, much in common with blood platelet research. This collection of records was rich in publications, in which commonly known mediators of cellular responses, such as platelet-derived growth factor (PDGF) [79], platelet-activating factor (PAF) [24] or platelet endothelial cell adhesion molecule (PECAM-1; CD31), had been used or studied [62]. Apart from the studies on blood platelets [25,80,81,82], various flavonoids (genistein, quercetin, apigenin, luteolin, isoliquiritigenin, catechins, baicalein, delphinidin and silybin) were used in experiments with smooth muscle cells [48,63,64,122], leukocytes [16,76], vascular endothelium [34], tumour cells [19], epithelium [7] or hepatocytes [108,115]. Flavonoids were used both for the assessment of cell functions and in order to trace the mechanisms underlying the cellular response.

The low specificity of the search strategy was also reflected by the relatively large number of journals with a broad scope, in which the analysed papers appeared. On the other hand, strategy #1 appeared to be the most sensitive among the initially considered options, as evidenced by the comparison between the numbers of records found using strategies #4 and #6 for 10 journals characterised by the highest numbers of the papers of interest.

On the basis of the analysis of publications determined with strategy #1, it can be claimed that in research on blood platelets, 98 genera of seed plants (*Spermatophyta*), belonging to 47 families, have been used. The highest percentages of described taxa concerned genera representing *Asteraceae*, *Fabaceae*, and *Rosaceae*, the largest seed plant families in the world [113]. Plant preparations used in platelet studies were isolated from various parts of the plant, namely: 1) rhizomes (e.g. *Pueraria lobata* (Willd.) Ohwi) [18], 2) seeds (e.g. *Vitis sp.*) [98], 3) roots (e.g. *Glycyrrhiza glabra* L.) [60], 4) flowers (e.g. *Prunus mume* Siebold & Zucc.) [120], 5) fruits (e.g. *Punica granatum* L.) [73], 6) bark (e.g. *Pinus pinaster* Aiton) [93], as well as 7) leaves (e.g. *Olea europaea* L.) [101]. Researchers were particularly interested in polyphenolic compounds contained in soy (mainly isoflavones), in beverages (tea, cocoa/chocolate, wine/grapes), in citrus fruits, in extracts from the bark of maritime pine (*Pinus pinaster* Aiton) and in extracts from ginkgo biloba (*Ginkgo biloba* L.). This was reflected in a large number of publications on this topic (original and review articles) and explains the seemingly low number of registered taxa in all the analysed papers.

In this study, we omitted the aspect of plant-originating drugs (Diosmin, Troxerutin, Legalon, Venostasin, Flavocoxid), which were also used in research on blood platelets and other cells. Moreover, during the construction of the taxonomical list, we deliberately excluded from the analysis herbal preparations developed according to traditional Chinese and Korean medicine. These included the DBT mixture (Danggui Buxue Tang) [27], extract from dragon's blood (*Daemonorops draco* BL.) [109], the extract Gua Lou Xie Bai Bai Jiu Tang [42], the seven-component mixture Hwaotang [89], as well as active substances isolated from *Panax notoginseng* (Burkill) F.H.Chen ex C.Y.Wu & K.M.Feng [28].

In this study, we were not able to perform a validated analysis of the association between the number of specific papers recorded in a particular year and the number of described genera/species. First, more than a single taxon was often described in a single publication. Second, in a particular year, a given taxon could be described several times in different papers, and/or the investigated extracts could originate from various parts of the same plant species (often with differing physico-chemical and biological properties). Furthermore, the content of polyphenols in plants may vary between species, and even between varieties of the same species [43]; thus it would be unwise to equate, for example, the extracts originating from the seeds or peels of grapes [98], resveratrol (biologically active compound isolated from *Vitis* sp.) [86] and wine [32], i.e. to treat these four specimens (preparations) as identical. Likewise, the oil obtained from olive [23] should not be identified with the extract isolated from the leaves of the same plant [101].

It should be emphasised that the compiled taxonomical list is based on strategy #1, which, unfortunately, does not fully cover the resources of PubMed. We were able to ascertain that strategy #1 did not exhaust the resources of PubMed thanks to using the auxiliary strategies (#5 option 1; #7 option 2) that enabled us to find other important (specific) records in PubMed. When creating the literature database, we noticed that searching with the use of the criterion "author" (option 3) might also improve the quality of a search.

In summary, the present study resulted in a list of taxa of the seed plants used in blood platelet research and revealed the basic features of a search strategy concerning the publications on flavonoids and blood platelets: high sensitivity, but quite low specificity. Even if the chosen strategies turn out not to be "perfect", we have indicated the ways of conducting an effective literature search in order to find as many taxonomic names as possible. Thus, it seems that the effective collection of literature requires the employment of various (often compounding) search options. Currently, the omnipresence of flavonoids in the diet, as well as their biological and therapeutic significance, are largely the hallmarks of their widespread usage in research.

References

[1] Abdel-Kader M.S.: Preliminary pharmacological study of the pterocarpans macckian and trifolirhizin isolated from the roots of *Ononis vaginalis*. Pak. J. Pharm. Sci., 2010; 23: 182-187

[2] Afifi F.U., Aburjai T.: Antiplatelet activity of *Varthemia iphionoides*. Fitoterapia, 2004; 75: 629-633

[3] Atta A.H., Elkoly T.A., Mouneir S.M., Kamel G., Alwabel N.A., Zaher S.: *Hepatoprotective effect of methanol extracts of Zingiber officinale* and *Cichorium intybus*. Indian J. Pharm. Sci., 2010; 72: 564-570

[4] Ben A.N., Bouaziz A., Romera-Castillo C., Salido S., Linares-Palomino P.J., Bartegi A., Salido G.M., Rosado J.A.: Characterization of the intracellular mechanisms involved in the antiaggregant properties of cinnamtannin B-1 from bay wood in human platelets. J. Med. Chem., 2007; 50: 3937-3944

[5] Beretz A., Briancon-Scheid F., Stierle A., Corre G., Anton R., Cazenave J.P.: Inhibition of human platelet cyclic AMP phosphodiesterase and of platelet aggregation by a hemisynthetic flavonoid, amentoflavone hexaacetate. Biochem. Pharmacol., 1986; 35: 257-262

[6] Carotenuto A., De F., V, Fattorusso E., Lanzotti V., Magno S., Cicala C.: The flavonoids of *Allium ursinum*. Phytochemistry, 1996; 41: 531-536

[7] Chan C.M., Huang J.H., Chiang H.S., Wu W.B., Lin H.H., Hong J.Y., Hung C.F.: Effects of (-)-epigallocatechin gallate on RPE cell migration and adhesion. Mol. Vis., 2010; 16: 586-595

[8] Chang C.L., Wang G.J., Zhang L.J., Tsai W.J., Chen R.Y., Wu Y.C., Kuo Y.H.: Cardiovascular protective flavonolignans and flavonoids from *Calamus quiquesetinervius*. Phytochemistry, 2010; 71: 271-279

[9] Chang F.R., Wei J.L., Teng C.M., Wu Y.C.: Antiplatelet aggregation constituents from *Annona purpurea*. J. Nat. Prod., 1998; 61: 1457-1461

[10] Chang W.C., Hsu F.L.: Inhibition of platelet activation and endothelial cell injury by flavan-3-ol and saikosaponin compounds. Prostaglandins Leukot. Essent. Fatty Acids, 1991; 44: 51-56

[11] Chang W.C., Hsu F.L.: Inhibition of platelet activation and endothelial cell injury by polyphenolic compounds isolated from *Lonicera japonica* Thunb. Prostaglandins Leukot. Essent. Fatty Acids, 1992; 45: 307-312

[12] Chaves D.S., Frattani F.S., Assafim M., de Almeida A.P., de Zingali R.B., Costa S.S.: Phenolic chemical composition of *Petroselinum crispum* extract and its effect on haemostasis. Nat. Prod. Commun., 2011; 6: 961-964

[13] Chen C.C., Huang Y.L., Sun C.M., Shen C.C.: New prenylflavones from the leaves of *Epimedium saggitatum*. J. Nat. Prod., 1996; 59: 412-414

[14] Chen J.J., Lee H.H., Shih C.D., Liao C.H., Chen I.S., Chou T.H.: New dihydrochalcones and anti-platelet aggregation constituents from the leaves of *Muntingia calabura*. Planta Med., 2007; 73: 572-577

[15] Cheng J., Kondo K., Suzuki Y., Ikeda Y., Meng X., Umemura K.: Inhibitory effects of total flavones of *Hippophae rhamnoides* L. on thrombosis in mouse femoral artery and *in vitro* platelet aggregation. Life Sci., 2003; 72: 2263-2271

[16] Chirumbolo S., Conforti A., Ortolani R., Vella A., Marzotto M., Bellavite P.: Stimulus-specific regulation of CD63 and CD203c membrane expression in human basophils by the flavonoid quercetin. Int. Immunopharmacol., 2010; 10: 183-192

[17] Chong M.F., Macdonald R., Lovegrove J.A.: Fruit polyphenols and CVD risk: a review of human intervention studies. Br. J. Nutr., 2010; 104, Suppl. 3: S28-S39

[18] Choo M.K., Park E.K., Yoon H.K., Kim D.H.: Antithrombotic and antiallergic activities of daidzein, a metabolite of puerarin and daidzin produced by human intestinal microflora. Biol. Pharm. Bull., 2002; 25: 1328-1332

[19] Chou D.S., Hsiao G., Lai Y.A., Tsai Y.J., Sheu J.R.: Baicalein induces proliferation inhibition in B16F10 melanoma cells by generating reactive oxygen species via 12-lipoxygenase. Free Radic. Biol. Med., 2009; 46: 1197-1203

[20] Chou H.C., Chen J.J., Duh C.Y., Huang T.F., Chen I.S.: Cytotoxic and anti-platelet aggregation constituents from the root wood of *Melicope semecarpifolia*. Planta Med., 2005; 71: 1078-1081

[21] Curtis P.J., Kroon P.A., Hollands W.J., Walls R., Jenkins G., Kay C.D., Cassidy A.: Cardiovascular disease risk biomarkers and liver and kidney function are not altered in postmenopausal women after ingesting an elderberry extract rich in anthocyanins for 12 weeks. J. Nutr., 2009; 139: 2266-2271

[22] De Bona K.S., Belle L.P., Sari M.H., Thome G., Schetinger M.R., Morsch V.M., Boligon A., Athayde M.L., Pigatto A.S., Moretto M.B.: *Syzygium cumini* extract decrease adenosine deaminase, 5'nucleotidase activities and oxidative damage in platelets of diabetic patients. Cell Physiol Biochem., 2010; 26: 729-738

[23] Dell'Agli M., Maschi O., Galli G.V., Fagnani R., Dal Cero E., Caruso D., Bosisio E.: Inhibition of platelet aggregation by olive oil phenols via cAMP-phosphodiesterase. Br. J. Nutr., 2008; 99: 945-951

[24] Dent G., Munoz N.M., Zhu X., Ruhlmann E., Magnussen H., Leff A.R., Rabe K.F.: Involvement of protein tyrosine kinases in activation of human eosinophils by platelet-activating factor. Immunology, 2000; 100: 231-237

[25] Deschamps J.D., Kenyon V.A., Holman T.R.: Baicalein is a potent *in vitro* inhibitor against both reticulocyte 15-human and platelet 12-human lipoxygenases. Bioorg. Med. Chem., 2006; 14: 4295-4301

[26] Dixon R.A., Ferreira D.: Genistein. Phytochemistry, 2002; 60: 205-211

[27] Dong T.T., Zhao K.J., Gao Q.T., Ji Z.N., Zhu T.T., Li J., Duan R., Cheung A.W., Tsim K.W.: Chemical and biological assessment of a chinese herbal decoction containing *radix Astragali* and *radix Angelicae sinensis*: determination of drug ratio in having optimized properties. J. Agric. Food Chem., 2006; 54: 2767-2774

[28] Dong T.T., Zhao K.J., Huang W.Z., Leung K.W., Tsim K.W.: Orthogonal array design in optimizing the extraction efficiency of active constituents from roots of *Panax notoginseng*. Phytother. Res., 2005; 19: 684-688

[29] El H.M., Bnouham M., Bendahou M., Aziz M., Ziyyat A., Legssyer A., Mekhfi H.: Inhibition of rat platelet aggregation by *Urtica dioica* leaves extracts. Phytother. Res., 2006; 20: 568-572

[30] Enomoto S., Okada Y., Guvenc A., Erdurak C.S., Coskun M., Okuyama T.: Inhibitory effect of traditional Turkish folk medicines on aldose reductase (AR) and hematological activity, and on AR inhibitory activity of quercetin-3-O-methyl ether isolated from *Cistus laurifolius* L. Biol. Pharm. Bull., 2004; 27: 1140-1143

[31] Facino R.M., Carini M., Franzoi L., Pirola O., Bosisio E.: Phytochemical characterization and radical scavenger activity of flavonoids from *Helichrysum italicum* G. Don (*Compositae*). Pharmacol. Res., 1990; 22: 709-721

[32] Folts J.D.: Potential health benefits from the flavonoids in grape products on vascular disease. Adv. Exp. Med. Biol., 2002; 505: 95-111

[33] Fujita T., Sakuma S., Sumiya T., Nishida H., Fujimoto Y., Baba K., Kozawa M.: The effects of xanthoangelol E on arachidonic acid metabolism in the gastric antral mucosa and platelet of the rabbit. Res. Commun. Chem. Pathol. Pharmacol., 1992; 77: 227-240

[34] Garcia-Alonso M., Rimbach G., Rivas-Gonzalo J.C., de Pascual--Teresa S.: Antioxidant and cellular activities of anthocyanins and their corresponding vitisins A - studies in platelets, monocytes, and human endothelial cells. J. Agric. Food Chem., 2004; 52: 3378-3384

[35] Garcia-Lafuente A., Guillamon E., Villares A., Rostagno M.A., Martinez J.A.: Flavonoids as anti-inflammatory agents: implications in cancer and cardiovascular disease. Inflamm. Res., 2009; 58: 537-552

[36] Gilani A.H., Mehmood M.H., Janbaz K.H., Khan A.U., Saeed S.A.: Ethnopharmacological studies on antispasmodic and antiplatelet activities of *Ficus carica*. J. Ethnopharmacol., 2008; 119: 1-5

[37] Grassi D., Desideri G., Croce G., Tiberti S., Aggio A., Ferri C.: Flavonoids, vascular function and cardiovascular protection. Curr. Pharm. Des, 2009; 15: 1072-1084

[38] Guglielmone H.A., Agnese A.M., Nunez Montoya S.C., Cabrera J.L.: Inhibitory effects of sulphated flavonoids isolated from *Flaveria bidentis* on platelet aggregation. Thromb. Res., 2005; 115: 495-502

[39] Guo Y., Fan L., Dong L.Y., Chen Z.W.: Effects of total flavone of *Abelmoschus manihot* (L.) Medik. on the function of platelets and its mechanism. Chin J. Integr. Med., 2005; 11: 57-59

[40] Gutierrez-Lugo M.T., Deschamps J.D., Holman T.R., Suarez E., Timmermann B.N.: Lipoxygenase inhibition by anadanthoflavone, a new flavonoid from the aerial parts of *Anadenanthera colubrina*. Planta Med., 2004; 70: 263-265

[41] Hara Y.: Tea catechins and their applications as supplements and pharmaceutics. Pharmacol. Res., 2011; 64: 100-104

[42] He X.J., Wang N.L., Qiu F., Yao X.S.: Research on active constituents research of gualou xiebai baijiutang (III). The active flavanoids. Zhongguo Zhong Yao Za Zhi, 2003; 28: 420-423

[43] Hubbard G.P., Wolffram S., Lovegrove J.A., Gibbins J.M.: The role of polyphenolic compounds in the diet as inhibitors of platelet function. Proc. Nutr. Soc., 2003; 62: 469-478

[44] Hwang S.B., Chang M.N., Garcia M.L., Han Q.Q., Huang L., King V.F., Kaczorowski G.J., Winquist R.J.: L-652,469 - a dual receptor antagonist of platelet activating factor and dihydropyridines from *Tussilago farfara* L. Eur. J. Pharmacol., 1987; 141: 269-281

[45] Ihantola-Vormisto A., Summanen J., Kankaanranta H., Vuorela H., Asmawi Z.M., Moilanen E.: Anti-inflammatory activity of extracts from leaves of *Phyllanthus emblica*. Planta Med., 1997; 63: 518-524

[46] Ikeda A., Inui K., Fukuta Y., Kokuba Y., Sugano M.: Effects of intravenous *Perilla* oil emulsion on nutritional status, polyunsaturated fatty acid composition of tissue phospholipids, and thromboxane A2 production in streptozotocin-induced diabetic rats. Nutrition, 1995; 11: 450-455

[47] Ikewuchi J.C., Onyeike E.N., Uwakwe A.A., Ikewuchi C.C.: Effect of aqueous extract of the leaves of *Acalypha wilkesiana* 'Godseffiana' Muell. Arg. (*Euphorbiaceae*) on the hematology, plasma biochemistry and ocular indices of oxidative stress in alloxan induced diabetic rats. J. Ethnopharmacol., 2011; 137: 1415-1424

[48] Ishizawa K., Izawa-Ishizawa Y., Ohnishi S., Motobayashi Y., Kawazoe K., Hamano S., Tsuchiya K., Tomita S., Minakuchi K., Tamaki T.: Quercetin glucuronide inhibits cell migration and proliferation by platelet-derived growth factor in vascular smooth muscle cells. J. Pharmacol. Sci., 2009; 109: 257-264

[49] Jantan I., Mohd Yasin Y.H., Jamil S., Sirat H., Basar N.: Effect of prenylated flavonoids and chalcones isolated from *Artocarpus* species on platelet aggregation in human whole blood. J. Nat. Med., 2010; 64: 365-369

[50] Jantan I., Raweh S.M., Sirat H.M., Jamil S., Mohd Yasin Y.H., Jalil J., Jamal J.A.: Inhibitory effect of compounds from *Zingiberaceae* species on human platelet aggregation. Phytomedicine, 2008; 15: 306-309

[51] Jonathan L.T., Gbeassor M., Che C.T., Fong H.H., Farnsworth N.R., Le Breton G.C., Venton D.L.: Pseudosemiglabrin, a platelet aggregation inhibitor from *Tephrosia semiglabra*. J. Nat. Prod., 1990; 53: 1572-1574

[52] Kelly G.S.: Quercetin. Monograph. Altern. Med. Rev., 2011; 16: 172-194

[53] Kim J.M., Yun-Choi H.S.: Anti-platelet effects of flavonoids and flavonoid-glycosides from *Sophora japonica*. Arch. Pharm. Res., 2008; 31: 886-890

[54] Kim K.H., Lee H.J., Lee J.H., Jang Y.S., Kim D.K., Shim B.S., Cho K.H., Ko S.G., Ahn K.S., Kim S.H.: Blockade of glycoprotein IIb/IIIa mediates the antithrombotic activity of butanol fraction of *Actinostemma lobatum* Maxim. J. Ethnopharmacol., 2008; 116: 431-438

[55] Kim Y.S., Pyo M.K., Park K.M., Park P.H., Hahn B.S., Wu S.J., Yun--Choi H.S.: Antiplatelet and antithrombotic effects of a combination of ticlopidine and *Ginkgo biloba* ext (EGb 761). Thromb. Res., 1998; 91: 33-38

[56] Ko H.H., Yu S.M., Ko F.N., Teng C.M., Lin C.N.: Bioactive constituents of *Morus australis* and *Broussonetia papyrifera*. J. Nat. Prod., 1997; 60: 1008-1011

[57] Koleckar V., Brojerova E., Rehakova Z., Kubikova K., Cervenka F., Kuca K., Jun D., Hronek M., Opletalova V., Opletal L.: *In vitro* antiplatelet activity of flavonoids from *Leuzea carthamoides*. Drug Chem. Toxicol., 2008; 31: 27-35

[58] Kolodziejczyk J., Olas B., Wachowicz B., Szajwaj B., Stochmal A., Oleszek W.: Clovamide-rich extract from *Trifolium pallidum* reduces oxi-

dative stress-induced damage to blood platelets and plasma. J. Physiol Biochem., 2011; 67: 391-399

[59] Kondo K., Suzuki Y., Ikeda Y., Umemura K.: Genistein, an isoflavone included in soy, inhibits thrombotic vessel occlusion in the mouse femoral artery and *in vitro* platelet aggregation. Eur. J. Pharmacol., 2002; 455: 53-57

[60] Kowalczyk E., Krzesinski P., Kura M., Niedworok J., Kowalski J., Blaszczyk J.: Pharmacological effects of flavonoids from Scutellaria baicalensis. Przegl. Lek., 2006; 63: 95-96

[61] Kuo S.C., Chen S.C., Chen L.H., Wu J.B., Wang J.P., Teng C.M.: Potent antiplatelet, anti-inflammatory and antiallergic isoflavanquinones from the roots of *Abrus precatorius*. Planta Med., 1995; 61: 307-312

[62] Kwon H.M., Choi Y.J., Choi J.S., Kang S.W., Bae J.Y., Kang I.J., Jun J.G., Lee S.S., Lim S.S., Kang Y.H.: Blockade of cytokine-induced endothelial cell adhesion molecule expression by licorice isoliquiritigenin through NF-κB signal disruption. Exp. Biol. Med., 2007; 232: 235-245

[63] Lamy S., Beaulieu E., Labbe D., Bedard V., Moghrabi A., Barrette S., Gingras D., Beliveau R.: Delphinidin, a dietary anthocyanidin, inhibits platelet-derived growth factor ligand/receptor (PDGF/PDGFR) signaling. Carcinogenesis, 2008; 29: 1033-1041

[64] Lamy S., Bedard V., Labbe D., Sartelet H., Barthomeuf C., Gingras D., Beliveau R.: The dietary flavones apigenin and luteolin impair smooth muscle cell migration and VEGF expression through inhibition of PDGFR-β phosphorylation. Cancer Prev. Res., 2008; 1: 452-459

[65] Lee C.L., Liao Y.C., Hwang T.L., Wu C.C., Chang F.R., Wu Y.C.: Ixorapeptide I and ixorapeptide II, bioactive peptides isolated from *Ixora coccinea*. Bioorg. Med. Chem. Lett., 2010; 20: 7354-7357

[66] Li H.X., Han S.Y., Wang X.W., Ma X., Zhang K., Wang L., Ma Z.Z., Tu P.F.: Effect of the carthamins yellow from *Carthamus tinctorius* L. on hemorheological disorders of blood stasis in rats. Food Chem. Toxicol., 2009; 47: 1797-1802

[67] Li S., Wang C.L., Guo S.X., Xiao P.G.: Advances in studies on chemical components and pharmacology of epiphytic type medicinal plants in the *Orchid* family. Zhongguo Zhong Yao Za Zhi, 2005; 30: 1489-1496

[68] Lin C.N., Kuo S.H., Chung M.I., Ko F.N., Teng C.M.: A new flavone C-glycoside and antiplatelet and vasorelaxing flavones from *Gentiana arisanensis*. J. Nat. Prod., 1997; 60: 851-853

[69] Ling S.K., Pisar M.M., Man S.: Platelet-activating factor (PAF) receptor binding antagonist activity of the methanol extracts and isolated flavonoids from *Chromolaena odorata* (L.) King and Robinson. Biol. Pharm. Bull., 2007; 30: 1150-1152

[70] Lo W.L., Wu C.C., Chang F.R., Wang W.Y., Khalil A.T., Lee K.H., Wu Y.C.: Antiplatelet and anti-HIV constituents from *Euchresta formosana*. Nat. Prod. Res., 2003; 17: 91-97

[71] Ma L., Wu F., Chen R.Y.: Advance of chemical constituents and bioactivity of *Saururuaceae* plants. Zhongguo Zhong Yao Za Zhi, 2003; 28: 196-198

[72] Martin K.R., Appel C.L.: Polyphenols as dietary supplements: A double-edged sword. Nutr. Diet. Suppl., 2010; 2: 1-12

[73] Mattiello T., Trifiro E., Jotti G.S., Pulcinelli F.M.: Effects of pomegranate juice and extract polyphenols on platelet function. J. Med. Food, 2009; 12: 334-339

[74] Mazza G.J.: Anthocyanins and heart health. Ann. Ist. Super. Sanita, 2007; 43: 369-374

[75] McKay D.L., Blumberg J.B.: Cranberries (*Vaccinium macrocarpon*) and cardiovascular disease risk factors. Nutr. Rev., 2007; 65: 490-502

[76] Mocsai A., Banfi B., Kapus A., Farkas G., Geiszt M., Buday L., Farago A., Ligeti E.: Differential effects of tyrosine kinase inhibitors and an inhibitor of the mitogen-activated protein kinase cascade on degranulation and superoxide production of human neutrophil granulocytes. Biochem. Pharmacol., 1997; 54: 781-789

[77] Murphy K.J., Chronopoulos A.K., Singh I., Francis M.A., Moriarty H., Pike M.J., Turner A.H., Mann N.J., Sinclair A.J.: Dietary flavanols and procyanidin oligomers from cocoa (*Theobroma cacao*) inhibit platelet function. Am. J. Clin. Nutr., 2003; 77: 1466-1473

[78] Mutanen M., Freese R., Valsta L.M., Ahola I., Ahlstrom A.: Rapeseed oil and sunflower oil diets enhance platelet *in vitro* aggregation and thromboxane production in healthy men when compared with milk fat or habitual diets. Thromb. Haemost., 1992; 67: 352-356

[79] Nakanishi H., Yamanouchi K., Gotoh Y., Nagayama M.: The association of platelet-derived growth factor (PDGF) receptor tyrosine phosphorylation to mitogenic response of human osteoblastic cells *in vitro*. Oral Dis., 1997; 3: 236-242

[80] Navarro-Nunez L., Lozano M.L., Martinez C., Vicente V., Rivera J.: Effect of quercetin on platelet spreading on collagen and fibrinogen and on multiple platelet kinases. Fitoterapia, 2010; 81: 75-80

[81] Navarro-Nunez L., Rivera J., Guerrero J.A., Martinez C., Vicente V., Lozano M.L.: Differential effects of quercetin, apigenin and genistein on signalling pathways of protease-activated receptors PAR1 and PAR4 in platelets. Br. J. Pharmacol., 2009; 158: 1548-1556

[82] Neuhaus T., Voit S., Lill G., Vetter H., Schror K., Weber A.A.: Platelet aggregation induced by the C-terminal peptide of thrombospondin-1 (4N1-1) is inhibited by epigallocatechin gallate but not by prostaglandin E1. Platelets, 2004; 15: 455-457

[83] Njamen D., Talla E., Mbafor J.T., Fomum Z.T., Kamanyi A., Mbanya J.C., Cerda-Nicolas M., Giner R.M., Recio M.C., Rios J.L.: Anti-inflammatory activity of erycristagallin, a pterocarpene from *Erythrina mildbraedii*. Eur. J. Pharmacol., 2003; 468: 67-74

[84] Okada Y., Miyauchi N., Suzuki K., Kobayashi T., Tsutsui C., Mayuzumi K., Nishibe S., Okuyama T.: Search for naturally occurring substances to prevent the complications of diabetes. II. Inhibitory effect of coumarin and flavonoid derivatives on bovine lens aldose reductase and rabbit platelet aggregation. Chem. Pharm. Bull., 1995; 43: 1385-1387

[85] Olas B., Kolodziejczyk J., Wachowicz B., Jedrejek D., Stochmal A., Oleszek W.: The extract from hop cones (*Humulus lupulus*) as a modulator of oxidative stress in blood platelets. Platelets, 2011; 22: 345-352

[86] Olas B., Wachowicz B., Saluk-Juszczak J., Zielinski T.: Effect of resveratrol, a natural polyphenolic compound, on platelet activation induced by endotoxin or thrombin. Thromb. Res., 2002; 107: 141-145

[87] Olas B., Wachowicz B., Tomczak A., Erler J., Stochmal A., Oleszek W.: Comparative anti-platelet and antioxidant properties of polyphenol--rich extracts from: berries of *Aronia melanocarpa*, seeds of grape and bark of *Yucca schidigera* in vitro. Platelets, 2008; 19: 70-77

[88] Ostertag L.M., O'Kennedy N., Kroon P.A., Duthie G.G., de Roos B.: Impact of dietary polyphenols on human platelet function - a critical review of controlled dietary intervention studies. Mol. Nutr. Food Res., 2010; 54: 60-81

[89] Park W.H., Park S.Y., Kim H.M., Kim C.H.: Effect of a Korean traditional formulation, Hwaotang, on superoxide generation in human neutrophils, platelet aggregation in human blood, and nitric oxide, prostaglandin E2 production and paw oedema induced by carrageenan in mice. Immunopharmacol. Immunotoxicol., 2004; 26: 53-73

[90] Pawlaczyk I., Czerchawski L., Kuliczkowski W., Karolko B., Pilecki W., Witkiewicz W., Gancarz R.: Anticoagulant and anti-platelet activity of polyphenolic-polysaccharide preparation isolated from the medicinal plant *Erigeron canadensis* L. Thromb. Res., 2011; 127: 328-340

[91] Piccinelli A.L., Garcia M.M., Armenteros D.M., Alfonso M.A., Arevalo A.C., Campone L., Rastrelli L.: HPLC-PDA-MS and NMR characterization of C-glycosyl flavones in a hydroalcoholic extract of *Citrus aurantifolia* leaves with antiplatelet activity. J. Agric. Food Chem., 2008; 56: 1574-1581

[92] Plotnikova A.M., Shulgau Z.T., Plotnikova T.M., Aliev O.I., Kulesh N.I., Mischenko N.P., Fedoreyev S.A.: Antithrombogenic and antiplatelet activities of extract from *Maackia amyrensis* wood. Bull. Exp. Biol. Med., 2009; 147: 204-207

[93] Putter M., Grotemeyer K.H., Wurthwein G., Araghi-Niknam M., Watson R.R., Hosseini S., Rohdewald P.: Inhibition of smoking-induced platelet aggregation by aspirin and pycnogenol. Thromb. Res., 1999; 95: 155-161

[94] Rui Y.C.: Advances in pharmacological studies of silymarin. Mem. Inst. Oswaldo Cruz, 1991; 86, Suppl. 2: 79-85

[95] Russo M., Spagnuolo C., Tedesco I., Bilotto S., Russo G.L.: The flavonoid quercetin in disease prevention and therapy: facts and fancies. Biochem. Pharmacol., 2012; 83: 6-15

[96] Saluk-Juszczak J., Pawlaczyk I., Olas B., Kolodziejczyk J., Ponczek M., Nowak P., Tsirigotis-Woloszczak M., Wachowicz B., Gancarz R.: The effect of polyphenolic-polysaccharide conjugates from selected medicinal plants of *Asteraceae* family on the peroxynitrite-induced changes in blood platelet proteins. Int. J. Biol. Macromol., 2010; 47: 700-705

[97] Samal A.B., Gabius H.J., Timoshenko A.V.: Galactose-specific lectin from *Viscum album* as a mediator of aggregation and priming of human platelets. Anticancer Res., 1995; 15: 361-367

[98] Shanmuganayagam D., Beahm M.R., Osman H.E., Krueger C.G., Reed J.D., Folts J.D.: Grape seed and grape skin extracts elicit a greater antiplatelet effect when used in combination than when used individually in dogs and humans. J. Nutr., 2002; 132: 3592-3598

[99] Silvan A.M., Abad M.J., Bermejo P., Villar A.: Effects of compounds extracted from *Santolina oblongifolia* on TXB(2) release in human platelets. Inflammopharmacology, 1998; 6: 255-263

[100] Silvan A.M., Abad M.J., Bermejo P., Villar A.: Effects of compounds extracted from *Tanacetum microphyllum* on arachidonic acid metabolism in cellular systems. Planta Med., 1998; 64: 200-203

[101] Singh I., Mok M., Christensen A.M., Turner A.H., Hawley J.A.: The effects of polyphenols in olive leaves on platelet function. Nutr. Metab Cardiovasc. Dis., 2008; 18: 127-132

[102] Skaltsa H., Bermejo P., Lazari D., Silvan A.M., Skaltsounis A.L., Sanz A., Abad M.J.: Inhibition of prostaglandin E2 and leukotriene C4 in mouse peritoneal macrophages and thromboxane B2 production in human platelets by flavonoids from *Stachys chrysantha* and *Stachys candida*. Biol. Pharm. Bull., 2000; 23: 47-53

[103] Stangl V., Lorenz M., Ludwig A., Grimbo N., Guether C., Sanad W., Ziemer S., Martus P., Baumann G., Stangl K.: The flavonoid phloretin suppresses stimulated expression of endothelial adhesion molecules and reduces activation of human platelets. J. Nutr., 2005; 135: 172-178

[104] Takano F., Tanaka T., Aoi J., Yahagi N., Fushiya S.: Protective effect of (+)-catechin against 5-fluorouracil-induced myelosuppression in mice. Toxicology, 2004; 201: 133-142

[105] Tao Y., Wang Y.: Bioactive sesquiterpenes isolated from the essential oil of *Dalbergia odorifera* T. Chen. Fitoterapia, 2010; 81: 393-396

[106] Tawata M., Aida K., Noguchi T., Ozaki Y., Kume S., Sasaki H., Chin M., Onaya T.: Anti-platelet action of isoliquiritigenin, an aldose reductase inhibitor in licorice. Eur. J. Pharmacol., 1992; 212: 87-92

[107] Tong Y., Zhou X.M., Wang S.J., Yang Y., Cao Y.L.: Analgesic activity of myricetin isolated from *Myrica rubra* Sieb. et Zucc. leaves. Arch. Pharm. Res., 2009; 32: 527-533

[108] Trappoliere M., Caligiuri A., Schmid M., Bertolani C., Failli P., Vizzutti F., Novo E., di M.C., Marra F., Loguercio C., Pinzani M.: Silybin, a component of sylimarin, exerts anti-inflammatory and anti-fibrogenic effects on human hepatic stellate cells. J. Hepatol., 2009; 50: 1102-1111

[109] Tsai W.J., Hsieh H.T., Chen C.C., Kuo Y.C., Chen C.F.: Characterization of the antiplatelet effects of (2S)-5-methoxy-6-methylflavan-7-ol from Draconis Resina. Eur. J. Pharmacol., 1998; 346: 103-110

[110] Tsai W.J., Hsin W.C., Chen C.C.: Antiplatelet flavonoids from seeds of *Psoralea corylifolia*. J. Nat. Prod., 1996; 59: 671-672

[111] Tsuchiya H.: Biphasic membrane effects of capsaicin, an active component in *Capsicum* species. J. Ethnopharmacol., 2001; 75: 295-299

[112] Vibes J., Lasserre B., Gleye J., Declume C.: Inhibition of thromboxane A2 biosynthesis in vitro by the main components of *Crataegus oxyacantha* (hawthorn) flower heads. Prostaglandins Leukot. Essent. Fatty Acids, 1994; 50: 173-175

[113] Ward L.K., Hackshaw A., Clarke R.T.: Do food-plant preferences of modern families of phytophagous insects and mites reflect past evolution with plants? Biol. J. Linn. Soc., 2003; 78: 51-83

[114] Willcox J.K., Catignani G.L., Lazarus S.: Tomatoes and cardiovascular health. Crit. Rev. Food Sci. Nutr., 2003; 43: 1-18

[115] Woo S.W., Lee S.H., Ko G., Kim Y.C., Sohn D.H.: Isoliquiritigenin inhibits cell proliferation by a heme oxygenase-dependent pathway in rat hepatic stellate cells. Planta Med., 2008; 74: 834-839

[116] Wright B., Moraes L.A., Kemp C.F., Mullen W., Crozier A., Lovegrove J.A., Gibbins J.M.: A structural basis for the inhibition of collagen-stimulated platelet function by quercetin and structurally related flavonoids. Br. J. Pharmacol., 2010; 159: 1312-1325

[117] Wu T.S., Chern H.J., Damu A.G., Kuo P.C., Su C.R., Lee E.J., Teng C.M.: Flavonoids and ent-labdane diterpenoids from *Andrographis paniculata* and their antiplatelet aggregatory and vasorelaxing effects. J. Asian Nat. Prod. Res., 2008; 10: 17-24

[118] Yang M., Chan G.C., Deng R., Ng M.H., Cheng S.W., Lau C.P., Ye J.Y., Wang L., Liu C.: An herbal decoction of radix *Astragali* and radix *Angelicae sinensis* promotes hematopoiesis and thrombopoiesis. J. Ethnopharmacol., 2009; 124: 87-97

[119] Yang Y., Andrews M.C., Hu Y., Wang D., Qin Y., Zhu Y., Ni H., Ling W.: Anthocyanin extract from black rice significantly ameliorates platelet hyperactivity and hypertriglyceridemia in dyslipidemic rats induced by high fat diets. J. Agric. Food Chem., 2011; 59: 6759-6764

[120] Yoshikawa M., Murakami T., Ishiwada T., Morikawa T., Kagawa M., Higashi Y., Matsuda H.: New flavonol oligoglycosides and polyacylated sucroses with inhibitory effects on aldose reductase and platelet aggregation from the flowers of *Prunus mume*. J. Nat. Prod., 2002; 65: 1151-1155

[121] Yu H.Y., Park S.W., Chung I.M., Jung Y.S.: Anti-platelet effects of yuzu extract and its component. Food Chem. Toxicol., 2011; 49: 3018-3024

[122] Yu J.Y., Lee J.J., Lim Y., Kim T.J., Jin Y.R., Sheen Y.Y., Yun Y.P.: Genistein inhibits rat aortic smooth muscle cell proliferation through the induction of p27kip1. J. Pharmacol. Sci., 2008; 107: 90-98

[123] Yu T., Chen Q.E., Chen Z.W., Xiong Z., Ye M.: Protective effects of total flavones of rhododendra against global cerebral ischemia reperfusion injury. Am. J. Chin Med., 2009; 37: 877-887

[124] Zhang J., Zheng Y., Han L.: Isolation of resisting thrombus and arteriosclerosis compounds in leaves of *Salix matsudana*. Zhong Yao Cai, 1999; 22: 131-133

[125] Zhao J., Zhang C.Y., Xu D.M., Huang G.Q., Xu Y.L., Wang Z.Y., Fang S.D., Chen Y., Gu Y.L.: The antiatherogenic effects of components isolated from pollen *Typhae*. Thromb. Res., 1990; 57: 957-966

The authors have no potential conflicts of interest to declare.