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THE USE OF *PANAX GINSENG* AND ITS ANALOGUES AMONG PHARMACY CUSTOMERS IN ESTONIA: A CROSS-SECTIONAL STUDY

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Abstract: The aim of the cross-sectional study was to evaluate the pattern of complementary self-treatment with *P. ginseng* and its analogues amongst pharmacy customers in Estonia. The study instrument consisted of multiple-choice items related to personal knowledge about and experience with the use of *P. ginseng* and its analogues. In total, 1233 customers participated in the study. Of study participants, 18.1% reported the use of *P. ginseng* and its analogues in their lives. *P. ginseng* preparations were used mostly according to the well-known indications (tiredness, weakness and decreased mental and physical capacity). Of *P. ginseng* users 44.3% reported positive treatment effects and 12.0% had experienced different side effects. With increase of age ($p < 0.01$) and at lower levels of education ($p = 0.04$), the use of ginseng or its analogues decreased. The better the users evaluated their health, the better they perceived the effect of *P. ginseng* preparations ($p < 0.01$). This study reported rather frequent use of *P. ginseng* and its analogues. *P. ginseng* could be seen in the treatment of conditions, where the use of local medicinal plants has not been established. Further research is needed to learn more about public knowledge and experiences about efficacy and safety of *P. ginseng* and its analogues.

Keywords: *Panax ginseng*, ginseng analogues, self-treatment, pharmacy customers

The root of the *Panax ginseng* Meyer has been a popular and widely used traditional herbal medicine in Asian countries for thousands of years. The popularity of *P. ginseng* as natural Chinese medicine has increased globally and currently it is frequently available in Western herbal preparations (1). *P. ginseng* is reported to have a wide range of therapeutic applications – it has beneficial effects on cardiovascular system, central nervous system, and immune system (2). Nevertheless, "there is clearly a lack of definitive evidence demonstrating any effects of *P. ginseng* on human physical and mental performance or any parameter related to perceived energy" (3, 4), nor the evidence to claim all health benefits and insure safety issues, as studies are often contradictory (4), which in fact is the case with many complementary and alternative medicines (CAM's) used worldwide (5). In addition to the contradictory clinical information about *P. ginseng*, only few international studies have focused on the user perception about *P. ginseng* (6).

P. ginseng arrived to Europe in the early Middle Ages through Arabian merchants. However, due to little awareness about medical properties of *P. ginseng*, it became known only since 17-th century. Nevertheless, medical doctors did not trust the miracle remedy and *P. ginseng* was not included to most European pharmacopoeias till 19-th century. A new wave of popularity of *P. ginseng* has grown during past fifty years.

According to the European Medicines Evaluation Agency (7), *P. ginseng*, as one-component preparation, has been available in different pharmaceutical formulations (tablets, powder, hard and soft capsules, oral liquid and herbal instant tea) in Germany, France and Sweden at least since middle of 1970s; in Austria, Ireland and Spain since 1980s and in Denmark, Poland and Portugal since 1990s. There is a large variability in the number of different *P. ginseng* preparations available on the market of different European countries starting with 60 different preparations in Germany and ending with one to two in Austria, Belgium, Denmark, Ireland and Portugal. In Italy and Latvia only combination preparations containing *P. ginseng* and/or vitamins, minerals and other components are available. According to regulatory status, *P. ginseng* preparations are granted marketing authorization as medicinal products in Austria, Belgium, Denmark, France, Germany, Ireland, Latvia, Poland, Portugal

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and Spain. *P. ginseng* preparations are considered as traditional preparations in Sweden and partly in Germany, Poland and Spain (7).

In Europe, *P. ginseng* is definitely one of the medicinal plants which have contributed to the adaptation of new exotic species into local CAM's (8). Similarly to the description given in several international studies about the use of *P. ginseng* (9-12), this medicinal plant is considered well-known and frequently used tonic available in community pharmacies also in Estonia.

Estonia, a small country in the Northern Europe, is one of the three Baltic States and bordering with Finland, Russia and Latvia. About 70% of its 1.3 million population are Estonian-speaking, while the rest of the population mostly speaks Russian as their mother-tongue. Estonia is known for intensive historical and modern use of local native and cultivated medicinal plants for self-medication of different minor conditions (13-17). In addition, foreign medicinal plants (such as *Mentha piperita, Chamomilla recutita, Calendula officinalis and Salvia officinalis*) have been adopted to the local culture or substituted with wild medicinal plants (18). There are several alternative means of information retrieval about the use of medicinal plants: traditions or literary sources, previous personal experience as well as information provided by healthcare professionals, usually pharmacist or doctor (19-21).

Based on its history and location, Estonia has been crossing of eastern and western culture and traditions. This could also be seen in the history of the use of *P. ginseng* in Estonia. *P. ginseng* is a good example of a foreign plant with no historical uses detected in earlier local folklore (22). *P. ginseng* as a wild species does not grow in Estonia and to date cultivation of this medicinal plant has not been established also (23). However, the *P. ginseng* preparations have been available at local community pharmacies starting from the last decades of 19-th century as the latest (24). At that time, Estonia was incorporated to the Russian Tsarist Empire. Russia, known as country with traditional guidelines for using *P. ginseng* (25), made these preparations also accessible in the western regions of its territory. During the First Republic of Estonia (1918–1940) the economic and cultural contacts were developed mostly with Western Europe and this could be one of the reasons, why *P. ginseng* was not available at community pharmacies, but was introduced again after the Second World War in the middle of 1950s, when Estonia was part of the Soviet Union (26). All *P. ginseng* preparations now available in Estonia are prepared from *P. ginseng*. While during Soviet period the promotion of medicinal products was unknown in Estonia, the commercials were available in mass-media after regaining of independence from the beginning of 1990s. In one of these commercials aged Chinese men demonstrated the human-like root of *P. ginseng* and introduced the ginseng preparations to the Estonian people.

There have been some analogues of *P. ginseng* such as *Eleutherococcus senticosus* (Rupr. & Maxim.), *Rhodiola rosea* L. (synonym *Sedum rosea* (L.) Scop.) and *Schisandra chinensis* (Turcz.) Baill., traditionally used during Soviet period (1940-1991) in Estonia (27) and/or tinctures, liquid extracts, tablets or capsules of described medicinal plants are available also in present time.

In some countries, including Estonia, ginseng has been perceived as a cultural representation of Chinese Medicine. Although, the medicine is well known and widely available, the public perception on the use of ginseng and its analogues are poorly studied in international literature.

To fill this knowledge gap, this study was aimed to evaluate the pattern of complementary self-treatment with *P. ginseng* and its analogues (*Eleutherococcus senticosus, Rhodiola rosea,* and *Schisandra chinensis*) amongst pharmacy customers in Estonia.

METHODS

Study design

Convenience sample of Estonian and Russian speaking pharmacy customers in three different towns of Estonia was used. Tartu (located in South-Estonia, population about 100,000) is the second biggest town in Estonia, where the majority of permanent residents are Estonian speaking. In the capital city of Estonia, Tallinn (located in North-Estonia, population about 400 000), the number of Russian speaking permanent residents is higher. In Kohtla-Järve (located in North-East Estonia close to Russian boarder, population about 40,000) a majority of the population are Russian speaking. In Tallinn, the study was undertaken in three community pharmacies in other two towns only one pharmacy was selected. All community pharmacies can be classified as medium size (approx. 30,000 prescriptions per year) pharmacies with large selection of non-prescription medicines and herbal products.

Two independent researchers conducted the study at the same period (June-August) in Tartu and Kohtla-Järve (2011) and in Tallinn (2012). In all community pharmacies customers approaching to the

counter of non-prescription medicines were invited to participate in the study. The research assistant explained the purposes of the study and oral informed consent was received from all interviewed pharmacy customers. In both, Tartu and Kohtla-Järve community pharmacies, 300 respondents were interviewed, in Tallinn 650 respondents were involved in the study. In total, 1250 pharmacy customers participated in the study. However, as 17 questionnaires were incomplete, the analysis was carried out with 1233 replies. The number of pharmacy customers which refused to participate in the study was not documented. For those respondents who never used *P. ginseng* or its analogues, only demographic data were collected. Respondents were interviewed in their native language (either Estonian or Russian) and only local residents participated in the study.

Study instrument

The study instrument was developed and discussed by a panel of researchers with a pharmaceutical background and extended knowledge in phytotherapy, ethnobotany, social pharmacy and semiotics. The study instrument applied was developed by using previous study models for evaluating self-medication with OTC medicines including medicinal plants (17, 20, 21, 28). A copy of the study instrument can be obtained from the corresponding author.

The study instrument consisted of multiple-choice items related to (1) personal knowledge or experience of the use of *P. ginseng*, (2) time and duration of the use, (3) specific preparation or form used, (4) purpose of the use and perceived effects, (5) mode of action and side effects of *P. ginseng* and its analogues, and (6) demographic characteristics of the respondent.

In Europe, *P. ginseng* preparations are used as a tonic in case of tiredness, weakness and decreased mental and physical capacity (7). These indications have been presented in package information leaflets of *P. ginseng* preparations marketed in Estonia and were pre-listed to assist respondents in selection of appropriate descriptions. In addition respondents could describe other indications, for what *P. ginseng* was used.

In addition to *P. ginseng* use, the study participants were asked to recall the use and efficacy of its analogues. Three different species were listed by their vernacular names in study instrument as to understand what analogues were used: *E. senticosus*, *R. rosea* and *S. chinensis*.

To assist the identification of the preparations nine different photos of preparations of *P. ginseng* available at the period of study were demonstrated to the respondents (Fig. 1). The pictures worked as triggers for activating mental herbal of the respondents (term proposed by Kołodziejska-Degórska) (29). Based on the experience of this study, several respondents recalled their use of *P. ginseng* only after seeing the pictures of the preparations. *P. ginseng* analogues were not illustrated with actual preparations.

Figure 1. Pictorial representations of the *P. ginseng* preparations which were available and were shown to the respondents during the interview: 1. Gerimax tablets of ginseng extract; 2. Gerimax tablets of ginseng extract with vitamins and minerals; 3. Gerimax liquid extract of ginseng; 4. Ginseng N liquid extract of ginseng; 5. Dynamisan tablets of ginseng extract; 6. Strong GinSeng tablets of ginseng extract; 7. Zhenchenya nastoika tincture of ginseng; 8. Vishpha tincture of ginseng; 9. Spectrum capsules of ginseng with vitamins, minerals, rutin and lecithin

The content validity and comprehensibility of the study instrument was pre-tested by ten randomly selected pharmacy customers of participating community pharmacy in Tartu. Minor changes to the wording of the items were made, based on feedback received.

This research did not use identifiable human material or data. The survey conforms to the Declaration of Helsinki and the ethical standards of Estonia. The researchers have fulfilled the Data Protection Act of Estonia.

Statistical analysis

Initial data were coded, inserted and stored in MS Excel database. For statistical analysis SPSS v. 10 was used and for calculation of statistical significance between demographic groups Pearson's χ^2 test was applied. Level of statistical significance was set at $p \leq 0.05$.

RESULTS

Frequency of *P. ginseng* and its analogues use

Of all study participants, 18.1% (n = 223) reported the use of *P. ginseng* of whom 49 respondents (4.0%) in addition consumed *P. ginseng* analogues in their lives (Table 1). Of the users, 48.9% (n = 109) had used *P. ginseng* preparation up to four years prior to the study, 31.4% (n = 70) five to ten years and 6.7% (n = 15) more than ten years ago. Described distribution could be seen as a signal about relatively recent popularity of *P. ginseng* in Estonia.

Of the *P. ginseng* users, 67.3% (n = 150) reported single and 32.7% (n = 73) repeat use of this medicinal plant. These results demonstrate rather medium interest towards *P. ginseng* preparations. However, the repeat use of *P. ginseng* preparations could be connected with positive effect of these preparations as only five study participants (6.8%) reported not having any effect and 30.1% (n = 22) could not determine the positive effect in case of multiple use of *P. ginseng*.

Duration of the use might also contribute to perceived satisfaction of selected preparation. Of the *P. ginseng* users, 38.6% (n = 86) consumed these preparations for more than one month during one course of the treatment, 35.4% (n = 79) for 2-3 weeks, 19.3% (n = 43) for less than a week and 6.7% (n = 15) claimed using *P. ginseng* more or less constantly.

The most popular of the three proposed species of *P. ginseng* analogues was *E. senticosus* (indicated 32 times). Rather popular was also *R. rosea* L. (22 times). To some extent *S. chinensis* was used less (named 5 times). Of the users of *P. ginseng* analogues 14.3% (n = 7) had used two and only 4.1% (n = 2) all three species of analogues.

Demographic data of non-users and users of *P. ginseng* were compared. With increase of age and among senior residents (both $p < 0.01$), people speaking Russian as native language ($p = 0.02$) and with lower levels of education ($p = 0.04$), the use of *P. ginseng* was less frequent. On the other hand, the use of *P. ginseng* was more common amongst working people and those with university degree and with better self-evaluated health ($p = 0.003$). Described results could be explained with reduced need for stimulants in older age and possible lack of awareness about exotic remedy among people with lower levels of education. More frequent use of *P. ginseng* in

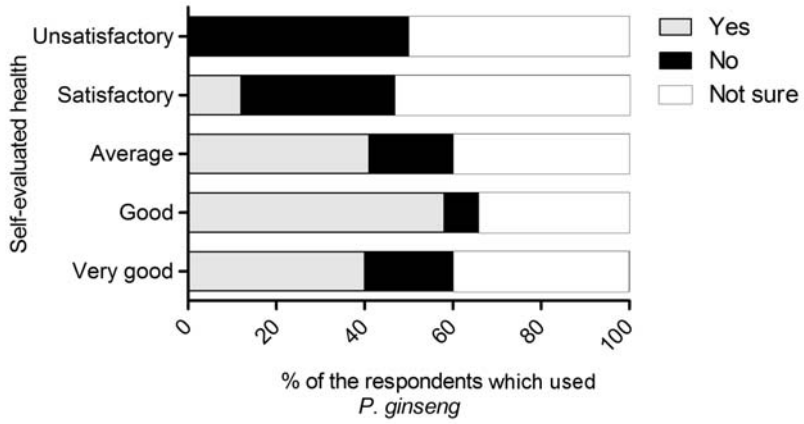

Figure 2. Self-evaluated health and perceived positive effect of *P. ginseng* preparations

Table 1. Socio-demographic characteristics of non-users and users of *P. ginseng*.

	Non-users n = 1010	%	Users n =223	%	Statistical significance ($p < 0.05$)
Age (years)					$p < 0.01$
16-30	250	24.8	46	20.6	
31-45	269	26.6	75	33.6	
46-60	205	20.3	65	29.1	
61-75	202	20.0	35	15.7	
75+	84	8.3	2	0.9	
Gender					ns
Female	665	65.8	158	70.9	
Male	345	34.2	65	29.1	
Education					$p = 0.04$
Elementary school	43	4.3	2	0.9	
High school	228	22.6	39	17.5	
Vocational education	288	28.5	70	31.4	
University degree	451	44.7	112	50.2	
Native language					$p = 0.02$
Estonian	621	61.5	158	70.9	
Russian	389	38.5	65	29.1	
Occupation					$p < 0.01$
Working	544	53.9	157	70.4	
Student	81	8.0	16	7.2	
Senior	267	26.4	29	13.0	
Unoccupied	61	6.0	6	2.7	
Working student	43	4.3	8	3.6	
Working senior	14	1.4	7	3.1	
Self-graded health					$p < 0.01$
Very good	167	16.5	24	10.8	
Good	458	45.3	107	48.0	
Average	230	22.8	73	32.7	
Satisfactory	134	13.3	17	7.6	
Unsatisfactory	21	2.1	2	0.9	
Place of interview					$p < 0.01$
Tartu	296	29.3	73	32.7	
Kohtla-Järve	297	29.4	43	19.3	
Tallinn Tõnismäe	202	20.0	37	16.6	
Tallinn Mustamäe	141	14.0	12	5.4	
Tallinn Pirita	297	29.4	58	26.0	

Tartu (known as a town with one of the oldest universities in Northern Europe) could be connected with higher number of inhabitants with university degree.

***P. ginseng* preparations used**

Of the 212 respondents which answered to the question, 75.0% (n = 159) claimed the use of only one specific *P. ginseng* preparation and 18.4% (n =

39) at least two different preparations. The rest of the respondents did not use preparations showed to them on the illustration or did not remember the specific preparations they used. Among the depictured preparations (Fig. 1) the most popular were tablets and solution containing *P. ginseng* as single component (no. 1-3) all together named 89 times and in combination with vitamins and minerals (no. 5), 13 times (Fig. 1). The pattern of those respondents reported only the use of mono-component *P. ginseng* preparations was similar to the all users of *P. ginseng*.

Selected preparations signal that a majority of the respondents reporting the use of *P. ginseng*, preferred to take tablets. The popularity of tablets was also confirmed by the parallel question addressing the preferred form of preparation, where tablets or capsules were used more frequently by 57.0% (n = 127) of the respondents and tinctures or liquid extracts by 20.2% (n = 45) of the respondents. More than half of the respondents, who had used tablets and capsules, reported positive effects of *P. ginseng* ($p = 0.032$).

Purpose of use and perceived effects of *P. ginseng* and its analogues

Of the respondents which used *P. ginseng*, 57.8% (n = 129) used those preparations for one and the rest for multiple indications. More popular single indications were general stimulation - 22.9% (n = 51), increase of mental capacity 17.0% (n = 38) and immune-stimulation 13.0% (n = 29). In addition, health recovery, increasing of appetite and blood pressure and antidepressant activity were mentioned by only few respondents. Of the multiple applications more popular were the combinations of general stimulation and an increase of mental capacity 13.5% (n = 30).

Despite whether *P. ginseng* preparations were used for single or multiple indications, only 46.2% (n = 103) of the respondents claimed that their health problem was solved; while 15.7% (n = 35) study participants reported that there was no effect. The rest of the respondents 38.1% (n = 85) could not evaluate if the *P. ginseng* preparation was effective or not.

Respondents who considered their health as very good, good or average experienced more positive effect of the *P. ginseng* intake than those with satisfactory or unsatisfactory self assessment of their health condition ($p < 0.01$) (Fig. 2). Rather surprisingly, residents of Tallinn experienced less positive effect of *P. ginseng* intake than residents of Tartu and Kohtla-Järve ($p = 0.03$). This may be related to speed-up living in Tallinn, the capital city of Estonia and hence probable higher expectations to a "miracle" medicine.

Of the *P. ginseng* analogue users, more than half (57.1%) claimed positive outcome of the treatment. The rest was not able to comment on the influence of the *P. ginseng* analogues on their health 34.7% (n = 17) or they did not experience any effect of its analogues 8.2% (n = 4).

Side-effects of *P. ginseng* preparations

Of the study participants used *P. ginseng*, 13.5% (n = 30) reported side effects. More frequent problems were 4.5% increased blood pressure (n = 10) and gastrointestinal tract irritation 3.6% (n = 8), but also anxiety 1.8% (n = 4), insomnia, arrhythmia and nasal bleeding 0.5% (n = 1). One respondent (0.5%) had experienced several side effects.

DISCUSSION

This is the first study in Estonia exploring the use for self-treatment and knowledge about exotic medicinal plants – *P. ginseng* and its analogues. The study results serve as a good example of newly introduced and widespread herbal product in Northern Europe.

Only few international studies have evaluated the frequency in the use of *P. ginseng* preparations. In those studies the number of respondents who have used *P. ginseng* within specified period of time varies within a wide range and is dependent on demographic characteristics. A study conducted among Sikh (Punjabi) community in London found the rate of citation to be 12% (11). This is still in times higher than in a study conducted in USA, where Cherniack and co-authors (12) found that 5% of the subset of respondents used *P. ginseng* preparations for self-treatment and the use rate among white population was even below 1%.

The high proportion of the users of *P. ginseng* detected in this study could be explained by covering the life-time period and questioning the respondents at the pharmacies, not covering the part of the population that do not attend pharmacies regularly. In Northern Europe *P. ginseng* combined with minerals was found to be particularly popular among Swedish women (6), but such preference was not confirmed by this study.

Priority given to tablets could be explained as well with the ease of taking ones, but also that tablets are culturally accepted form of medicine in Estonia for already longer period of time. Although the intake of liquids in form of medicinal teas is

rather common in Estonia (16), the intake of tinctures containing alcohol appears to be of less cultural importance. It could be explained with tinctures and infusions contain most often alcohol, which can influence the ability to drive, although the quantities are small.

In this study, the popularity of *P. ginseng* and its perceived effects as a stimulant is worthy of attention, demonstrating rather well defined position of the *P. ginseng* preparations within the herbal landscape of Estonians. The use of stimulants in Estonian traditional medicine is not common or at least it was not perceived as such, although immune-stimulation could be seen as one of the reasons to use medicinal plants for prevention of cold and cold relate diseases, which was rather popular already in 19th century (17, 22).

The perception of the study participants on the safety and the side effects of ginseng corresponds with former international research that has described *P. ginseng* as herbal preparation with a good safety profile and low incidence of adverse effects (30) and a double-blind, placebo-controlled, parallel group clinical study reported mild adverse events as dyspepsia, hot flash, insomnia and constipation in both placebo and P. ginseng group subjects (31).

Study limitations

The study did not include the entire population, but only the samples of pharmacy customers in three different regions of Estonia. However, community pharmacies are the most frequent places where one can purchase *P. ginseng* preparations in Estonia and selected study sample and setting created the foundation for collecting the reliable information.

The selection of illustrated *P. ginseng* preparations was limited to those available at community pharmacies at the time of the study. This could be the reason why the participants who had used *P. ginseng* preparations more than five years ago did not recall correctly the used preparation.

CONCLUSIONS

This study gives initial information about lay perception and use of *P. ginseng* and its analogues, based on the sample of pharmacy customers in North-European country Estonia. Based on the results, the sample customer of *P. ginseng* is a middle aged (31-60 years) Estonian female with university degree and a good health.

In comparison with other studies and considering the region, the use of *P. ginseng* was rather frequent – about 1/5 of the study participants. *P. ginseng* preparations were used mostly according to the well-known indications - tiredness, weakness and decreased mental and physical capacity. Thus, *P. ginseng* could be seen as a helping tool in the treatment of such conditions, where the use of traditional medicinal plants of Estonia has not been well-established (e.g., mental stimulation).

The efficacy of *P. ginseng* and its analogues was evaluated similarly – about half of the users experienced positive effects, 1/3 could not determine the effects and the rest did not experience any improvement of their condition. Described outcomes support the results of international studies about inconsistency of *P. ginseng* efficacy. On the other hand, evaluation of the efficacy of analogues on the similar level with more studied *P. ginseng* demonstrate existing practical experience of Estonian pharmacy customers about the use of different exotic medicinal plants.

Although the study gives a short overview concerning the frequency and content of side effects experienced by *P. ginseng* users, the future research has to concentrate more on the safety aspects (interactions, contraindications) of *P. ginseng* and its analogues.

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