

# Menopausal Women In South Italy: Assumption Of Soy Isoflavone Based Products, Effects And Interference With Levothyroxine Treatment

Rita Patrizia Aquino<sup>1,2</sup>, Manuela Grimaldi<sup>1</sup>, UldericoDe Martino<sup>1</sup>, Paola Sabatini<sup>3</sup>, Antonio Grasso<sup>1</sup>,  
Anna Maria D'Ursi<sup>1,2\*</sup>

1. Department of Pharmacy, Pharma Nomics Interdepartmental Center.

2. Osservatorio interdipartimentale per gli Studi di Genere e le Pari Opportunità (OGEPO), University of Salerno, Via Giovanni Paolo II, 132, I-84084 Fisciano (SA), Italy.

3. U.O.C. Clinical Pathology D.E.A. III Umberto I, Nocera Inferiore, Salerno, Italy.

## RESEARCH

Please cite this paper as: Rita Patrizia Aquino, Manuela Grimaldi, Massimo UldericoDe Martino, Paola Sabatini, Antonio Grasso, Anna Maria D'Ursi. Menopausal Women In South Italy: Assumption Of Soy Isoflavone Based Products, Effects And Interference With Levothyroxine Treatment. Women's Health Research [2018] 1(1): 1-8.

### \*Corresponding Author:

Anna Maria D'Ursi

Osservatorio interdipartimentale per gli Studi di Genere e le Pari Opportunità (OGEPO), University of Salerno, Via Giovanni Paolo II, 132, I-84084 Fisciano (SA), Italy.

Email: [dursi@unisa.it](mailto:dursi@unisa.it); [magrimaldi@unisa.it](mailto:magrimaldi@unisa.it)

## ABSTRACT

### Background

Menopause is a physiological condition that all women experience as a normal part of aging which main symptoms are hot flashes, insomnia, night sweats, vaginal dryness, moodiness, and irritability. However, women in menopause may have unfavourable levels in several risk factors for osteoporosis and cardiovascular diseases. This study was carried out to determine the effect of soy isoflavone dietary supplements in reducing menopause symptoms and in causing potential side effects in a population of women from Salerno District, Campania Region, South Italy.

### Methods

Personal data, reasons for the soy isoflavone assumption, menopausal symptoms and their improvements by isoflavones intake as well as potential undesirable effects were recorded using a structured questionnaire. Data were analysed by the OLAP method (Online Analytical Processing).

### Results

Data from a total of 117 women (sample A) in menopause over three year's period were analysed. The age of the participants ranged from 39 to 68 years. A subset of the target population (53 participants, sub-sample B) suffered from thyroid dysfunction and co-assumed isoflavones supplements and levothyroxine.

The participants used soy isoflavones supplements in response to the advice of the pharmacist (44% in B compared to 37% in A), medical prescription (32% in B compared to 36% in A) whereas marketing advertising or for self-medication account for 24% in B and 27% in A.

102 participants (87.18% of A) described an improvement of menopause syndrome; all symptoms disappeared in 46.85% of sample A and 51.22% of sub-sample B. Interestingly, hot flashes, sweating and moodiness decreased in 20.72, 12.61 and 10.81% of A, respectively, and in very similar manner in B. Fifteen women described no improvement of menopause syndrome, and two out these participants reported gastrointestinal disorders. Eight participants reported very mild undesired effects. Worthy of notice five out the above eight undesired effects were registered in sub-sample B.

### Conclusion

The effective of soy isoflavone supplements in improving quality of life seems to be substantially high in women in menopause and only slight side effects were registered, mainly in the sub-sample taking levothyroxine. Efforts to minimize the problem by accurate information should be promoted and provided to women as well as a careful monitoring of so-called "natural" supplements.

**Key Words:** Menopause; Soy isoflavone supplements, Beneficial effects; Un desired effects; Campania Region, Salerno District.



## Introduction

Menopause is a period of woman life, lasting 7-14 years, characterized by the decrease in the secretion of sexual hormones, in particular oestrogens and progesterone. [1-5] Due to the influence of these hormones in a great number of metabolic pathways, the progressive reduction of their secretion in menopause has serious consequences, in particular on the cardiovascular system. Vasomotor syndrome characterized by intense hot flashes, flushing, night sweats or even severe symptoms represented by chronic insomnia, osteoporosis, early atherosclerosis [3-5] require a consistent pharmacological treatment based on hormone therapy, [6-8] to improve the quality of life.

An alternative to the hormone therapy is represented by natural therapies with "phytoestrogens". [9] Soy isoflavones are phytoestrogens exerting estrogenic agonistic, partially agonist or even antagonist activity; as such they are able to interact with the oestrogen cellular target. Due to the estrogenic potency 1.000 to 10.000 times lower than estradiol, phytoestrogens are used as mild and harmless dietary supplements, considered natural substitutes of estrogenic therapy for the control of menopausal symptoms in women. As all products containing plant-based derivatives, phytoestrogens have their specific pharmacological and toxicological effects; however, their safety profile is still questionable. In particular soy isoflavones may influence physiopathological conditions and their pharmacokinetic and pharmacodynamics profile may cross over with food and synthetic drugs, affecting positively or negatively their efficacy. [10-12]

Consumption of food supplements is recently increased owing to the growing attention to disease prevention. In consequence research on these topics is boosted, in view of the development of effective health products based on modern food technologies. [13] However, market analysis often shows that the consumer of food supplements is not aware of the potential adverse health effects related to inappropriate use, where the use of such products should take place in a conscious and, above all, informed manner.

In this context, phyto-surveillance is an indispensable tool for a correct assessment of the risks associated with the use of food supplements containing bioactive plant-derived products. Indeed, the estimation of the risk/benefit ratio related to the assumption of phyto-therapeutic products is strictly recommended when these products are ingested concurrently with synthetic drugs necessary to cure different pathologies. [14-16]

In the last years, thyroid diseases have been increasing incidence in Italy. [17] Own to probable

phenomena of environmental pollution, this incidence is particularly high in the Campania region. In these cases, levothyroxine drug is largely used as therapy to protect thyroid gland in patients suffering from thyroid dysfunction. In view of the prevalent incidence of thyroid dysfunctions among women they are considered "gender" disease. Hashimoto's thyroiditis, the most common cause of hypothyroidism, is an autoimmune disorder in which antibodies directed against the thyroid gland lead to chronic inflammation. Hashimoto's thyroiditis occurs most commonly in middle aged women and several evidences have shown that soy isoflavones may interfere with thyroid pathologies and their therapies. [18-20] Accordingly, ingestion of integrators containing soy isoflavones may affect the pharmacokinetic of thyroid hormones, with unexpected effects in the thyroglobulin secretion, T3, T4 and TSH production. [21-25] To avoid possible interference between phyto-therapy and hormonal therapy, the prescription of soy isoflavone supplements as remedies for menopausal symptoms requires the application of severe phyto-surveillance protocols, for the women in hormonal therapy for thyroid dysfunction.

In the present study we analysed 117 women living pre-menopausal, menopausal or post-menopausal period, suffering from the typical menopausal symptoms and assuming phytoestrogens deriving from soy in nutraceutical commercial products. We evaluated the ability of the commercial products to reduce the menopausal symptoms and to induce potential side effects. Moreover, in a subset of women in treatment with hormonal therapy for thyroid dysfunction, we investigated the occurrence of possible interferences of nutraceutical products with the hormonal therapy.

## Materials and Methods

A survey was carried out among women population in menopause assuming soy isoflavone-based products living in South of Italy, Campania Region, Salerno District, aged from 39 to 68 years at 30 pharmacies and 2 drugstores.

A sample of 117 women (participants) were recruited and monitored in the period July 2015- July 2017. Study related information was provided by pharmacists and women signed informed consent prior to participation in the study. Characteristics of all subjects are shown in Table 1.

107 of them were in menopausal period, the others in pre-menopause. Criterion of recruitment was the treatment with dietary supplements composed of soy isoflavones and assumed as remedies for the menopausal symptoms (sample A). A subset of the target population (sub-sample B) met the second criteria of interest; infact they suffered from thyroid dysfunction and assumed



isoflavones supplements in co-assumption with levothyroxine. Criterion of exclusion was woman age lower than 39 and higher than 68, the presence of pathologies other than thyroid dysfunction.

A specific questionnaire (herbal supplement monitoring form HSMF) for monitoring type of products, effects on menopause symptoms and potential adverse drug reactions (ADRs) was developed and administered to the sample. The questionnaire included the following sections: Section A, Personal Data in anonymous form (age, gender, ethnic origin, geographic region, presence or absence of thyroid dysfunction); Section B, Type and commercial name of the product; Motivation/reasons for the soy isoflavone assumption (self-medication, publicity by different media, medical prescription, pharmacist recommendation); Section C, menopausal syndrome by a list of possible symptoms and any improvements registered; Sections D and E, dedicated to the reporting of eventual simultaneous other pathologies which may be a cause of exclusion from the trial; Section F, dedicated to the reporting of any undesirable effects recorded during the course of soy isoflavone intake. A pilot survey of 10 women was performed prior to the main study. The questionnaires were distributed from July 2015 to September 2016. The aim of the study was to explore use of supplements, motivations to use, menopausal symptoms before and after intake during a minimum of one-month, beneficial effects post-intake, undesired effects post-intake. The main outcome was the experience of menopausal treatment with isoflavone supplements among the women, assessed as the number of women who had benefits and perceived or feared side effects. Secondary outcomes were the same experience in participants co-assuming levothyroxine.

### Data Analysis

Data obtained from the survey were elaborated by the OLAP method (Online Analytical Processing). OLAP is a computer-based technique of data warehouse design and analysis which allows answering multi-dimensional queries swiftly; OLAP leads users to analyse multidimensional data interactively from multiple perspectives (in our case woman, product, symptoms, effect, adverse effect, etc.). [26-29]

## Results and Discussion

### Sample A -Effects of soy isoflavones in menopause symptoms

In the Sections A and C of the questionnaire, the women reported their anagraphical data, general health conditions with particular attention to assumption of other drugs, particularly levothyroxine, pre- or -menopausal state

and perceived symptoms. Table 2 reports the women sample stratified by age and the relative menopausal symptomatology. As shown in Fig. 1, the data indicate the highest incidence of typical menopausal symptoms for the cohort aged between 49 and 58. These symptoms are less perceived in the pre-menopausal (39-48 ages) and post-menopausal (59-68 ages) cohorts.

In the section B, registering the products and the reasons for the soy isoflavone assumption, most women stated that information regarding isoflavones was obtained from a medical doctor (36%) or a pharmacist (37%). Other sources of information were internet and traditional media which account for a total of 22%; only 5% reported an assumption for self-medication.

In the Section C the women were invited to answer questions regarding their treatment with isoflavone food supplement and possible effects on the menopause. Table 3 reports the data relative to the self-reported improvement deriving from the intake of soy isoflavone food supplements on each menopausal symptom. Soy isoflavone determined a general improvement of the menopausal syndrome in 102 out of 117 participants, whereas 15 women described no amelioration. As reported in Fig. 2, some participants out of 117 women reported improvement of only one symptom - hot flashes in 24 women (20.72%), - mood swings in 13 (10.81%), - sweating in 15 (12.61%). Worthy of notice, roughly half of surveyed women (about 47%) indicated a marked improvement for all perceived symptoms. Only few women reported an improvement in palpitation, vaginal dryness, insomnia and sense of swelling (Table 3).

### Sample A - Side effects

Section F of the questionnaire included questions relative to any undesired effects recorded during the use of soy isoflavone-based products. Accordingly, it was possible to record improvement, no change, or worsening for each symptom. Moreover, it was possible to highlight specific undesirable effects. Results show that two of the 15 women who indicated no improvement in menopausal symptoms also reported gastrointestinal disorders resulting from the intake of the soy isoflavone supplements; whereas 8 of 102 women who reported improvements in symptoms related to menopausal syndrome, recorded a total of eight side effects, in particular fatigue, weight gain, diarrhoea, difficulty in the digestion, tiredness, tachycardia, swelling, intolerance. (Table 4)

### Sub-sample B – women in treatment with levothyroxine

Our sample included the sub-sample B corresponding to 53 women in menopausal period using soy isoflavones and, simultaneously, in treatment with levothyroxine for thyroid disease. Sub-sample B1 was represented by the women of sample B in treatment with



the leader product among the soy isoflavone products available in the market segment analysed.

The women of sub-sample B were encouraged to use soy isoflavones in response to the advice of the pharmacist (24), medical prescription (17), marketing advertising (10), or for self-medication (2). It is interesting to observe that sub-sample B shows the more relevant impact of the pharmacist's advice that counts for 44% (compared to 37% in A) in comparison to the medical prescription that was indicated in 32% of the sub-sample B (compared to 36% in A)(Fig. 3).

Analysis of the questionnaires from sub-sample B evidenced that the perceived menopause symptoms are distributed as follows: flushes (N. 44 registrations), mood swings sweating (N.41), (N. 38 registrations), palpitations (N. 32), vaginal dryness (N. 37), insomnia (N. 2), high blood pressure (N. 1). Therefore, the comparison with the data of the sample A indicates that the effects perceived on the menopausal symptom are very similar in the whole sample and the related subset accounting for - flushes (19.51%), - mood swings (9.76%), - sweating (12.20%). The perceived improvement for all symptoms was recorded in 27 women representing 51.22% of sub-sample B. In analogy to what recorded for the entire sample A, only one woman out of 53 referred an attenuation of the swelling, or palpitation, or vaginal dryness or insomnia (Table 3 and Fig. 2).

One of the 9 women who indicated no improvement in menopausal symptoms also described the effect of unwanted "gastrointestinal disorders" (1/53 women). Five out of the 53 women (17%) who reported improvements in symptoms related to menopausal syndrome mentioned as side effects, weight gain, fatigue, tachycardia, swelling, and diarrhoea. (Table 4)

All together results suggested that:

- i) All the symptoms of menopause were perceived as improved and/or reduced (Table 3) by the women who participated to the trial following the intake of the soy isoflavone supplements;
- ii) Among all the symptoms, the vasomotor syndrome (hot flashes, sweating etc.) is the most significantly improved in both samples A and B. Side effects (fatigue, weight gain, diarrhoea, tachycardia and swelling) were rarely reported in women, suffering from thyroid disease and using levothyroxine. In rare cases difficulties in the digestion, gastrointestinal disorders, fatigue, and intolerance to the product were experienced during the period of supplement intake. For these cases investigation of the food intake habits could provide additional elements to distinct the interference strictly related to soy-isoflavone and hormonal therapy and those possibly related to diet. However the combination of data that more than half of our women sample experienced an improvement in all menopausal syndrome and about 88% detected improvement in one or

a combination of symptoms confirms that soy isoflavones may be an effective method to control menopausal syndrome as reported in the literature.<sup>9, 30</sup> However, in some cases undesirable effects may emerge. Therefore, an active phyto-vigilance seems to be essential to adequately assess the risk/benefit ratio in soy isoflavone products assumption. [31-34]

## Conclusion

Our results are in line with increasing evidence relative to the chemistry, pharmacology, and clinic effects of soy isoflavones and their ability to reduce climacteric symptoms; however, you cannot rule out the possibility that they, like all natural and synthetic products and drugs, are not free of side effects and potential drug interactions.

Finally, this study may pave the way to the following important perspectives:

- i) The promotion of a culture of reporting undesirable effects and/or adverse events, not only from drugs, but also from food supplements; this particularly in the population suffering from chronic diseases and subjected to regular pharmacological therapy;
- ii) The importance to collect information and updates on food supplements for pharmacists and healthcare operators;
- iii) The use of OLAP method [26] in phyto-vigilance field to design easily analysable data ware house instead of analysing, as usually happens, data collected by means of not fully rationalized models;
- iv) The promotion of innovative tools to access information and disseminate an appropriate use of phyto-therapeutic and food supplements.

The aim of active phyto-vigilance research is to increase the benefits, reduce the risks, to gain an overall improvement of people health in using food supplements having positive effects on the National Health System.

## References

1. Dennerstein L, Lehert P, Guthrie JR, Burger HG, Modeling women's health during the menopausal transition: a longitudinal analysis. *Menopause*, 2007. 14: p. 53-62.
2. Nelson H, Taylor B, Weatherall I, *Lancet*. *Menopause*, 2008. 371: p. 760-770.
3. Dennerstein L, Dudley EC, Hopper JL, Guthrie JR, Burger HG, A prospective population-based study of menopausal symptoms. *Obstet Gynecol*, 2000. 96: p. 351-358.
4. Ayers B, Forshaw M, Hunter MS, The impact of attitudes towards the menopause on women's symptom experience: a systematic review. *Maturitas*, 2010. 65: p. 28-36.
5. Sturdee DW, The menopausal hot flush—anything new? *Maturitas*, 2008. 60: p. 42-49.
6. Deborah B, Remer, Symptoms of the menopause. *Best*





Pract Res Clin Obstet Gynaeco, 2009. 23(1): p. 25-32.

7. Nelson HD, Humphrey LL, Nygren P, Teutsch SM, Allan JD, Postmenopausal hormone replacement therapy: scientific review. JAMA, 2002. 288: p. 872-881.

8. Tissier R, Waintraub X, Couvreur N, et al; Pharmacological post conditioning with the phytoestrogen genistein. J Mol Cell Cardiol, 2007. 42: p. 79-87.

9. Setchell K, Phytoestrogens: the biochemistry, physiology, and implications for human health of soy isoflavones. Am J Clin Nutr, 1998. 68: 1333S-1346S.

10. Crowell J, Levine B, Page J, Preclinical safety studies of isoflavones. J Nutr, 2000. p. 130.

11. D'Adamo CR, Sahin A, Soy foods and supplementation: a review of commonly perceived health benefits and risks. Altern Ther Health Med, 2014. P. 39-51.

12. Song WO, Chun OK, Hwang I, et al; Soy isoflavones as safe functional ingredients. J Med Food. 2007. 10:571-580.

13. FederSalus. Il ruolo dell'integrazione alimentare in farmacia. Position Paper. 2018.

14. Greendale GA, FitzGerald G, Huang M-H, et al; Dietary soy isoflavones and bone mineral density: results from the study of women's health across the nation. Am J Epidemiol, 2002. 155: p. 746-754.

15. Park SA, Choi M-S, Cho S-Y, et al; Genistein and daidzein modulate hepatic glucose and lipid regulating enzyme activities in C57BL/KsJ-db/db mice. Life sci, 2006. 79: p. 1207-1213.

16. This P, De Cremoux P, Leclercq G, Jacquot Y. A critical view of the effects of phytoestrogens on hot flashes and breast cancer risk. Maturitas. 2011. 70: p. 222-226.

17. Dal Maso L, Panato C, Franceschi S, et al; The impact of over diagnosis on thyroid cancer epidemic in Italy, 1998–2012. Eur J Cancer, 2018. 94: p. 6-15.

18. Marotta V, Sciammarella C, Chiofalo MG, et a;. Hashimoto's thyroiditis predicts outcome in intrathyroidal papillary thyroid cancer. Endocr Relat Cancer, 2017. 24: p. 485-493.

19. Jabbar MA, Larrea J, Shaw RA, Abnormal thyroid function tests in infants with congenital hypothyroidism: the influence of soy-based formula. J Am Coll Nutr, 1997.16: p. 280-282.

20. Chorazy PA, Himelhoch S, Hopwood NJ, Greger NG, Postellon DC, Persistent hypothyroidism in an infant receiving a soy formula: case report and review of the literature. Pediatrics, 1995. 96: p. 148-150.

21. Divi RL, Chang HC, Doerge D, Anti-thyroid isoflavones from soybean: isolation, characterization, and mechanisms of action. Biochem Pharmacol, 1997. 54: p. 1087-1096.

22. Doerge DR, Sheehan DM, Goitrogenic and estrogenic activity of soy isoflavones. Environ Health Perspect, 2002.

23. Dos Santos MCdS, Gonçalves CFL, Vaisman M, Ferreira ACF, de Carvalho DP, Impact of flavonoids on thyroid function. Food Chem Toxicol, 2011. 49: p. 2495-2502.

24. Bell M, FACE, David SH, Ovalle M, Fernando, Use of soy

protein supplement and resultant need for increased dose of levothyroxine. Endocr Pract, 2001. 7: p. 193-194.

25. Sathyapalan T, Manuchehri AM, Thatcher NJ, et al; The effect of soy phytoestrogen supplementation on thyroid status and cardiovascular risk markers in patients with subclinical hypothyroidism: a randomized, double-blind, crossover study. J Clin Endocrinol Metab, 2011. 96: p. 1442-1449.

26. Corrente M, Grasso A, Vilecco F, D'Amore M, Aquino R, Phytovigilance of Soy Isoflavones Products: Use of the Business Intelligence for Designing Efficient Monitoring Forms. 2015. 3(1): p. 1-7.

27. Han J, Pei J, Kamber M, Data mining: concepts and techniques. Elsevier, 2011.

28. Pendse N. The OLAP report-what is olap.1999.

29. Kocakoç ID, Erdem S, Business intelligence applications in retail business: OLAP, data mining & reporting services. Journal of Information & Knowledge Management. 2010. 9: p. 171-181.

30. Moreira AC, Silva AM, Santos MS, Sardão VA, Phytoestrogens as alternative hormone replacement therapy in menopause: What is real, what is unknown. J Steroid Biochem Mol Biol, 2014.143: p. 61-71.

31. B Gencil V, M Benjamin M, N Bahou S, A Khalil R, Vascular effects of phytoestrogens and alternative menopausal hormone therapy in cardiovascular disease. Mini Rev Med Chem, 2012. 12: p. 149-174.

32. Hassan HA, Abdel-Wahhab MA. Effect of soybean oil on atherogenic metabolic risks associated with estrogen deficiency in ovariectomized rats. J Physiol Biochem, 2012. 68: p. 247-253.

33. Heaney RP, Weaver CM, Fitzsimmons ML, Soybean phytate content: effect on calcium absorption. The American Am J Clin Nutr, 1991. 53: p. 745-747.

34. Mei J, Yeung SS, Kung AW, High dietary phytoestrogen intake is associated with higher bone mineral density in postmenopausal but not premenopausal women. J Clin Endocrinol Metab, 2001. 86: p. 5217-5221.

## PEER REVIEW

Not commissioned. Externally peer reviewed.

## CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

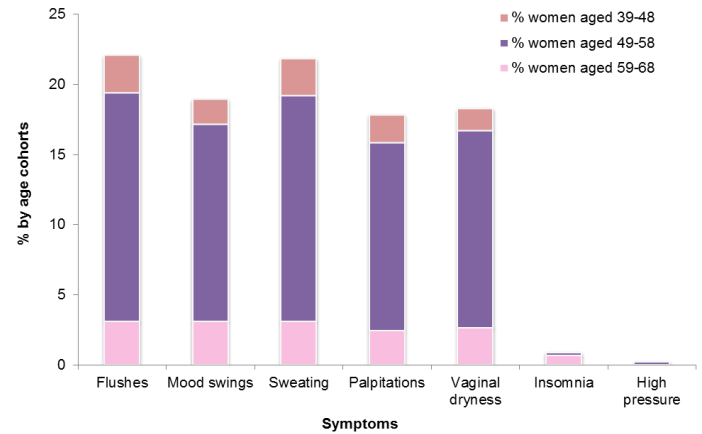


## TABLES AND FIGURES

**Table 1:** Characteristics of the Study Population.

<b>N° total of participants</b>	117
<b>Pre-menopause</b>	10
<b>Menopause</b>	107
<b>Participants without Thyroid dysfunction</b>	64
<b>Participants with Thyroid dysfunction</b>	53
<b>Age range of the participants</b>	
<b>39-48 years</b>	19
<b>49-58 years</b>	80
<b>59-68 years</b>	18

**Fig. 1:** Percentage of each menopausal symptom by age cohorts in the sample (A) of women under examination.



**Table 2:** Main menopausal symptoms and percentage incidence by age cohort in the participants (sample A).

Symptom	N. women Total	%	N. women aged 59-68	N. women aged 49-58	N. women aged 39-48
Flushes	99	<b>22.05</b>	14 (3.12%)	73 (16.26%)	12 (2.67%)
Mood swings	85	<b>18.93</b>	14 (3.12%)	63 (14.03%)	8 (1.78%)
Sweating	98	<b>21.83</b>	14 (3.12%)	72 (16.04%)	12 (2.67%)
Palpitations	80	<b>17.82</b>	11 (2.45%)	60 (13.37%)	9 (2.00%)
Vaginal dryness	82	<b>18.26</b>	12 (2.67%)	63 (14.03%)	7 (1.56%)
Insomnia	4	<b>0.89</b>	3 (0.67%)	1 (0.22%)	0 (0.00%)
High pressure	1	<b>0.22</b>	0 (0.00%)	1 (0.22%)	0 (0.00%)

**Table 3:** Improvement of menopausal symptoms in the participants (sample A, sub-sample B and B1) after soy isoflavone intake.

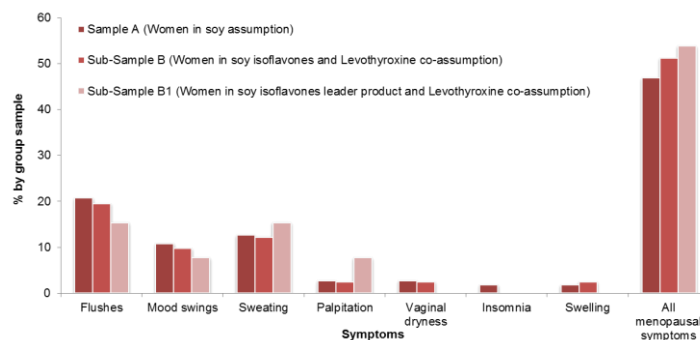
SUMMARY OF THE IMPROVEMENT OF MENOPAUSAL SYMPTOMS			
Groups	Sample A	Sub-Sample B**	Sub-Sample B1**
Symptoms	Percentage of improvement		
Flushes	24 (20.72%)	11 (19.51%)	2 (15.38%)
Mood swings	13 (10.81%)	5 (9.76%)	1 (7.69%)
Sweating	15 (12.61%)	7 (12.20%)	2 (15.38%)
Palpitation	3 (2.70%)	1 (2.44%)	1 (7.69%)
Vaginal dryness	3 (2.70%)	1 (2.44%)	-----
Insomnia	2 (1.80%)	-----	-----
Swelling	2 (1.80%)	1 (2.44%)	-----
All menopausal symptoms	55 (46.85%)	27 (51.22%)	6 (53.85%)

\* Women taking soy isoflavones

\*\* Women taking soy isoflavones and Levothyroxine

\*\*\* Women taking soy isoflavones leader product and Levothyroxine

**Fig. 2:** Incidence of menopausal symptoms improvement after intake of soy isoflavone products in the three test groups.



**Table 4:** List of side effects that emerged during the trial.

TYPE AND NUMBER OF UNDESIRE EFFECTS REGISTERED DURING THE TRIAL			
Undesired effect	N. Women on total sample* (117)	N. Women of Sub-Sample B** (53)	N. Women of Sub-Sample B1*** (12)
SAMPLE	A	B	B1
Fatigue	1	1	1
Weight gain	1	1	-
Diarrhea	1	1	-
Difficulty in digestive phase	1	-	-
Tiredness	1	-	-
Tachycardia	1	1	-
Swelling	1	1	-
Intolerance	1	-	-
No symptomatic improvement after soy isoflavones assumption	15	9	1
	of which N. 2 also reporting Gastrointestinal disorders	of which N. 1 also reporting Gastrointestinal disorders	

\* Women taking soy isoflavones

\*\* Women taking soy isoflavones and Levothyroxine

\*\*\* Women taking soy isoflavones leader product and Levothyroxine

**Fig. 3:** Percentage of soy isoflavones use in response to the advice of the pharmacist, medical prescription, marketing advertising and for self-medication, in the Sample A and in the Sub-Sample B.

