

Food Supplements Usage During Covid-19 Pandemic

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Abstract:

Millions of people worldwide use food supplements to maintain their body wellbeing and for immune boosting mainly against flu or other seasonal infections. Taking into consideration the great importance given to the use of supplements during COVID-19 pandemic, the aim of this study is to evaluate the importance and precaution of supplements and herbal products usage for immunity boosting during COVID-19 pandemic in Tirana region, Albania. According to the pharmacists, there is a wide range of supplements used during COVID-19 pandemic. One of the most used supplements in Albania during COVID-19 pandemic, was the combination of Vitamin C, Vitamin D3 direct and Zinc, a product from FORTEX nutraceuticals in the form of dispersible sachets for oral intake without water. Combinations of Vitamin D and Vitamin K are used also.

Based on these facts, vitamin D level was measured in a group of 2295 randomly chosen individuals, presented in the laboratory for routine analysis. Compared to the data from previous studies during the period from 2009-2010, where a mean value of 21.49 (\pm 7.6) ng/ml for vitamin D was observed, there is a slight increase in vitamin D concentration from 2019-2022, with a mean value of 24.14 (\pm 9.07) ng/ml. Regardless the extra care and supplements intake, the range varies from 8-67 ng/ml and the level of vitamin D insufficiency is still high in the population.

More than 87% of the individuals were taking supplements regularly, during COVID-19 pandemic. 57% of them were aware that interactions between supplements and medications could occur. The persons who were informed that interactions could occur were part of age group from 18-45 years old. About 21% of them approved that the pharmacist has always asked them about other medications or supplements they were administering in addition to those they buy to the pharmacy. Pharmacists recommend also taking medications and supplements at least an hour apart and to keep a diary about any side effects that come on along with supplements use. It is important to avoid using supplements that contain large amounts of ingredients too.

Keywords: COVID-19, food supplements, consumer awareness, vitamin D, herbal products

Introduction

The use of dietary supplements (DSs) has been steadily increasing all over the world for the last decades, and approximately 50–75% of populations have taken them routinely, and almost half of them—regularly (Hamulka J. Et al. 2020; Cowan AE Et al.2018; Sekhri K & Kaur K, 2014; Barnes K. Et al, 2016 and Czerwiński, A., Liebers, D. 2019). According to Grand View Research on “Dietary Supplements Market Size, Share & Trends Analysis Report By Ingredient (Vitamins, Minerals), By Form, By Application, By End User, By Distribution Channel, By Region, And Segment Forecasts, 2022 – 2030.”, accessed on April 7th, 2022; the global dietary supplements market size is expected to expand at a compound annual growth rate of 8.9% from 2022 to 2030. Increasing consumer awareness toward personal health and wellbeing is expected to be a key driving factor for dietary supplements over the forecast period.

Food supplements are mainly used to help our regular diet by correcting nutritional deficiencies and maintain mainly microelements, vitamins and minerals or other nutrients that are essential in biochemical reactions and improve different physiological functions. They are essential in poor diet or when the human body, for different reasons cannot take sufficient quantities of essential nutrients. The most used and common food supplements are vitamins, amino acids and minerals. According to the European Food Safety Authority, dietary supplements are intended to correct nutritional deficiencies, maintain an adequate intake of certain nutrients, or support specific physiological functions. According to a study conducted in Lithuania, based on two samples of adults from Lithuania, the first in 2019 and the second in 2021, the consumption of dietary supplements was prevalent among 67.2% and 78.1% of the samples, respectively (Hamulka J. Et al. 2020); which shows an increase of food supplements usage during the pandemic period. Another study conducted in Poland showed that the consumption of dietary supplements containing zinc and vitamin D increased during the pandemic, especially among people with higher education (59.0%), or those with medical and paramedical education (54.5%) (Hamulka J. Et al. 2020; Puścion-Jakubik A, Et al. 2021).

A study on the trends in Dietary Supplement Use among US Adults From 1999–2012 (Kantor ED. Et al. 2016) showed that supplement use was associated with several socio-demographic variables. For example, supplement use increased with age, with 72% of adults ages 65+ reporting use (95% CI: 69%, 75%), as compared to 40% of adults ages 20–39 (95% CI: 35%, 45%). Women (58%; 95% CI: 55%, 62%) were also more likely to use supplements than men (45%; 95% CI: 42%, 49%). Considering the variation in supplement use across Europe (Flynn, A., Et al. 2009; Skeie, G., Et al. 2019), supplements vary in the contribution that they make to food-sourced intake and the proportion of the populations at risk of not meeting the sufficiency dietary reference value (DRVs) (Lentjes M. A. H. 2019).

According to another study and the statistics presented by NCHS data, February 2021 U.S. Department Of Health And Human Services Centers For Disease Control And Prevention National Center For Health Statistics, Dietary supplement use increased with age, overall and in both sexes, and was highest among women aged 60 and over (80.2%). From this study is noticed that in all age groups, the highest percentage of dietary supplements goes to multivitamin-mineral, which in the age group of 60 and over, represents 39.4% of the total food supplements intake. Vitamin D is the second most used food supplement after multivitamin-mineral in all age groups, reaching the maximal value in the age group of 60 and over. Regarding the amount of food supplements usage in comparison to age, it is noticed that from the age group of 20-39 to the age group of 40-59, the amount of supplements is almost two times more and when comparing to the age group of 60 and over, the amount of

supplements used is three times more compared to the age group 20-39. Regarding the purpose of dietary supplements usage, in a study on COVID-19 Pandemic and Consumption of Dietary Supplements among Adult Residents of Lithuania (Arlauskas R. Et al, 2022), most of the dietary supplements are taken by people for the overall strengthening of the body.

There are few studies conducted in this field in our country. According to a study conducted in 2014 on knowledge and awareness of nutritional supplements and drug interactions (Bebeçi E. Et al, 2015), 71% of the patients were using nutritional supplements and among them 39.5% were aware of nutritional supplement interactions with drugs/medications. A recent study, held in 2021 in Albania, on dietary supplement consumption by Albanian consumers, was focused on the frequency, reasons for use, expectations of food supplements usage and the level of awareness on the use of dietary supplements. The primary purpose of using supplements for Albanian consumers was energy increasing in 39% of the responders and immunity improvement in 38.1% of the responders (Peçuli A. Et al, 2022). It must be mentioned that the information for this study was collected based on an online distributed questionnaire. Taking into consideration the focus and the importance given to food supplements usage during pandemic, this study aims to evaluate the actual situation on food supplements intake and the level of awareness between patients regarding the food supplements-drugs interaction or adverse effects when taken in the same time.

Method

This study is focused on the assessment of the importance of food supplements intake and level of awareness between patients presented in the pharmacy for their medications, in Tirana during the period of time from 2019-2021. The patients were asked to fulfil a questionnaire (distributed to patients with the help of pharmacists), where general data for the patient were recorded, like: age, gender, educational background and certainly the main focus was the use of food supplements, knowledge on the interaction between food supplements and drugs, etc. The patients were asked also whether their pharmacist asked them about the administration of drugs and food supplements in the same time.

In order to evaluate the possible effects of food supplements intake in our health, the status of vitamin D in a randomly chosen group was tested. 2295 randomly chosen individuals, 1657 women and 638 men, during the same period (2019-2021) were included in these study. A 10 ml fasting blood sample was collected in pre-chilled tubes for determination of PTH, 1, 25–dihydroxyvitamin D and electrolytes. Serum concentration of 25(OH) D were measured by VIDAS bioMérieux. VIDAS® is a reliable and easy-to-use automated benchtop immunoanalyzer. The assay principle combines an enzyme immunoassay competition method with a final fluorescent detection (ELFA). Based on the Enzyme Linked Fluorescent Assay (ELFA) technology, it provides high quality on-demand test results. The reference range includes four different statuses of vitamin D, such as deficient (<20ng/ml); insufficient (20-29 ng/ml); sufficient (30-100 ng/ml) dhe potential toxicity (>100 ng/ml). These recommendations for vitamin D levels are given based to the most recent literature suggestions.

Results and Discussion

A random group of 750 patients/individuals presented at the pharmacy to receive their treatments, were asked about the supplements they used and about the knowledge, they had about these supplements. Taking into account the importance given to the use of vitamins D and C as well as the administration of some special ions such as zinc, iron, magnesium, etc. during the pandemic, in this study we aim to evaluate the knowledge and awareness linked to

supplements usage from the patients or people presented in the pharmacy. This study is focused only in this source of supplements taken in pharmacies, without taking into account other sources of vitamins and microelements or other nutrients intake from fortified foods, special food regime, etc.

In table 1 we present some general data related to patients/people presented routinely in the pharmacy.

Table 1. Number and percentage of survey population by age group

| Parameter | Total number (%) | Mean ± SD | P value |
|--------------------------|-------------------------|------------------|----------------|
| Age group (years) | | | |
| 18-24 | 350 (47 %) | 10.3±4.79 | 0.033 |
| 25-39 | 103 (13.7 %) | 11.8±4.52 | |
| 40-59 | 135 (18%) | 10.91±4.77 | |
| 61+ | 162 (21.6%) | 10.95±3.92 | |
| Gender | | | |
| Female | 427 (57%) | 10.37±4.22 | 0.01 |
| Male | 323 (43%) | 11.53±4.73 | |
| Residence area | | | |
| Rural area | 278 (37%) | 11.34±4.1 | 0.002 |
| Urban area | 472 (63%) | 10.32±4.79 | |
| Education | | | |
| Primary school degree | 37 (5%) | 11.79±3.79 | 0.032 |
| Secondary school degree | 105 (14%) | 10.87±4.45 | |
| High school degree | 608 (81%) | 9.97±4.2 | |
| Marital status | | | |
| Single | 429 (57.2%) | 10.5±4.15 | 0.73 |
| Married | 246 (32.8%) | 9.7±3.72 | |
| Widow | 21 (2.8%) | 11.4±4.3 | |
| Divorced | 54 (7.2%) | 11.7±4.9 | |

From the table above, we notice that women are more predisposed to use food supplements (57%) compared to men (43%). From the analysis of the total number of individuals included in this survey, it results that more than 87 % of the group was taking supplements regularly, before (for prevention reasons and strengthening of the immune system), during and after the infection with COVID-19. About 80% of them claim to have used food supplements at least once. 57% of them were informed that interactions between supplements and medications could occur. When they were asked further and in more details about the effects that food supplements can have when combined with drugs, even those who had no knowledge about these interactions, started to think about possible interaction between food supplements and drugs when taken at the same time. It is reflected also on the percentage of people who answered that: “It depends on the combination supplements-medication”.

Table 2. Knowledge of the individuals, on the effects resulting from supplement-medication interactions

| Frequency | Answers |
|-----------|--|
| 1.18% | There are no effects |
| 7.69% | There are positive effects caused |
| 14.79% | There are negative effects caused |
| 5.92% | I don't know |
| 70.41% | It depends on the combination supplements-medication |

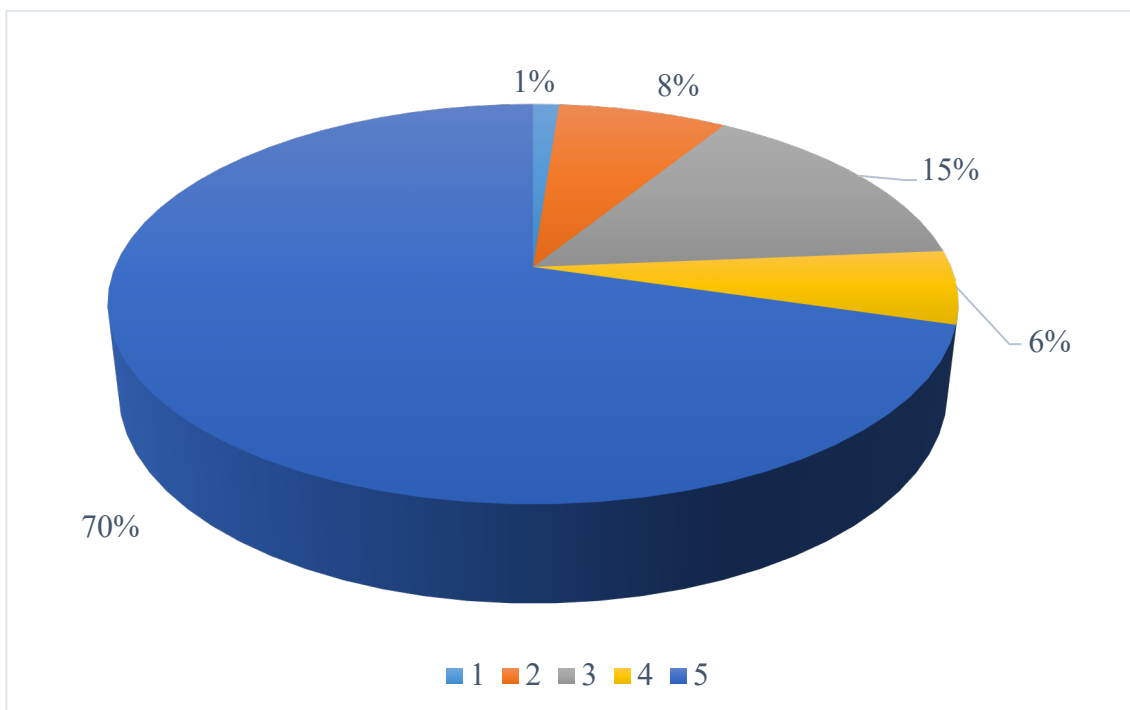


Figure 1. Knowledge of the individuals, on the effects resulting from supplement-medication interactions

People who were more informed that interactions could happen were mostly in the 18-24 and 25-39 age group (respectively 22% and 20%). About 21% of them approved that the pharmacist has always asked them about other medications or supplements they are administering in addition to those they buy at pharmacy.

Table 3. Knowledge on the effect of drug-supplements interaction, if taken in the same time

| Frequency | Individuals were asked if taking supplements and drugs at the same time would have an effect |
|-----------|--|
| 5.56% | Affects the increase of the effect of the supplement |
| 6.67% | Affects the reduction of the effect of the supplement |
| 8.89% | It does not affect the increase or decrease of their effect at all |
| 11.67% | Affects the increase of the effect of the drug |
| 11.67% | Affects the reduction of the effect of the drug |
| 12.22% | Affects the reduction of the effect of both |
| 17.78% | Affects the increase of the effect of both |
| 25.56% | I don't know |

As we can see from the table and the distribution of answers between people/patients about the possible effects caused by drug-supplements interaction and the way this interactions affect us, 25.56 % of the individuals included in this survey had no information about that. In these conditions we can say that there is still a lot of work to be done in terms of raising people's awareness about the use and combination drug-supplements.

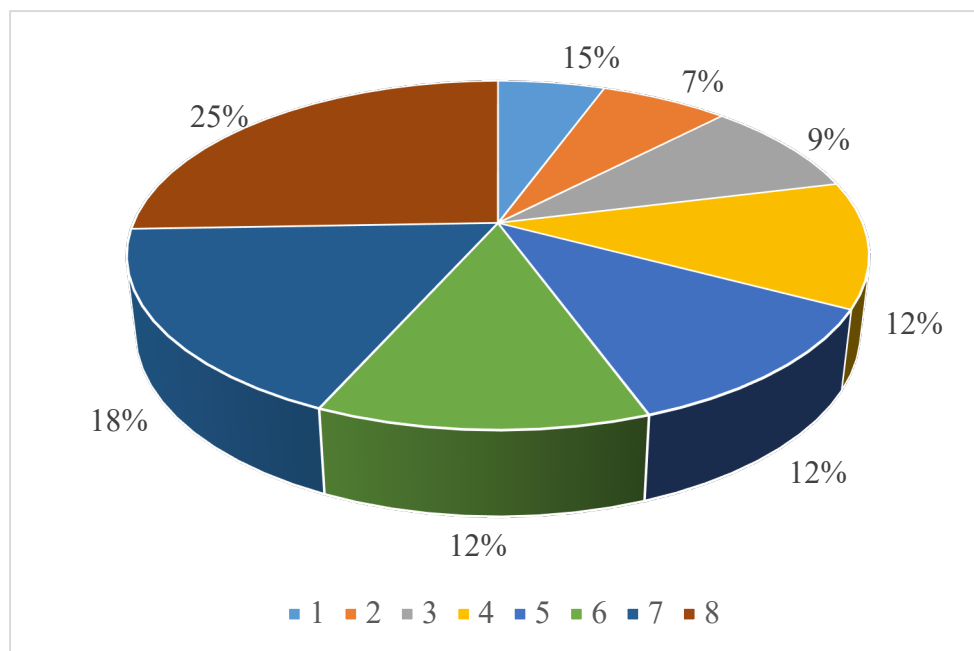


Figure 2. Distribution of answers on the effect of drug-supplements interaction, if taken in the same time

Table 4. Most common types of dietary supplements used during 2019-2021

| Frequency | Supplement type |
|-----------|----------------------------|
| 78% | Multivitamins and minerals |
| 84% | Vitamin D |
| 75% | Vitamin C |
| 38% | Omega 3 fatty acids |
| 9% | Vitamin B ₁₂ |

From the answers to the questionnaires, results that the most popular supplements used during pandemic were: multivitamins and minerals (zinc, magnesium and iron) observed in 78% of the cases, followed by vitamin D and C (taken by 84% and 75% of the responders respectively), Omega 3 fatty acids/fish oil was taken by a considerable percentage of the people (38%) and vitamin B₁₂, taken mostly by the age group over 60 in the form of injection. According to a study on dietary supplements during COVID-19 outbreak, the most frequently used supplements globally, are magnesium, vitamin D, iron, honey, and vitamin B₁₂. The same study shows similar findings in Poland, where the five most popular compounds were magnesium, vitamin D, honey, vitamin C, and iron (Hamulka J. Et al, 2020).

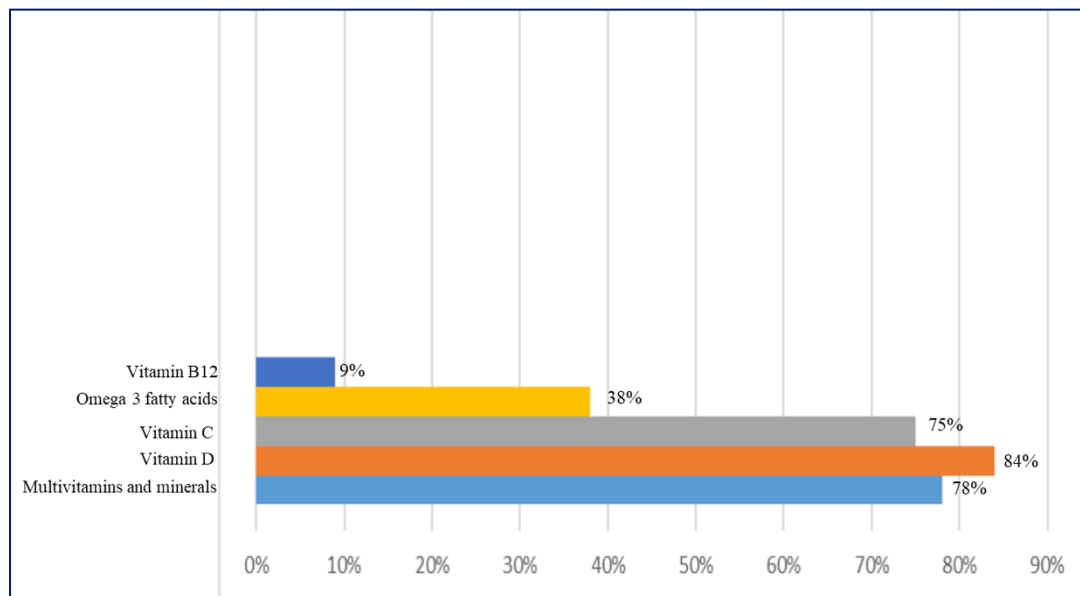


Figure 3. Most common types of dietary supplements used during 2019-2021

Vitamin D is one of the supplements that has the best level of evidence compared to other food supplements and according to the pharmacists, one of the most used supplements in Albania during the pandemic of COVID-19, was the combination of Vitamin C, Vitamin D₃ direct and Zinc, a product from FORTEX nutraceuticals in the form of dispersible sachets for oral intake without water. Combinations of Vitamin D and Vitamin K are used also. Although vitamin K is beneficial in helping with vitamin D, to those taking blood thinners, taking vitamin K may cause the opposite effect to the therapy, therefore in these cases it is not recommended by the pharmacist.

Melatonin was one of the supplements used more rarely from people facing sleep disorders and anxiety about one hour before bedtime. This treatment was effective for some people and not effective to others, so herbal products were another alternative for insomnia and anxiety treatment. Based on the tradition of use of medicinal plants, different medicinal plants are used in the form of tincture or infusion, or essential oils as well. A combination of *Melissa officinalis*, *Origanum marjorana* and *Pelargonium graveolens* was used as infusion to treat insomnia and anxiety. *Ocimum basilicum* or *Matricaria chamomilla* infusion was used for the same purpose widely. *Salvia officinalis*, fresh and dried, was used widely for its anti-inflammatory effects. *Eucalyptus rostrata* or *Laurus nobilis* oil is used as a broncho dilator widely in the population and is taken three times a day before meals as a supplement for the treatment of COVID-19 symptoms at home. Black seed (*Nigella sativa* seeds) is used as tea three times a day in order to boost the immunity and prevent the infection.

Based on information from available studies, there are supplements with a low risk of clinically important interactions such as *Actaea racemosa*, *Vaccinium* spp., *Ginkgo biloba*, *Panax quinquefolius*, *Silybum marianum*, *Serenoa repens*, *Valeriana officinalis* (Fuchikami H, Et al. 2006; Patel NM& Derkits RM, 2007; Stoddard GJ, Et al. 2015; Yuan CS, Et al. 2004; Han Y, Et al.2009) and those with a high risk of clinically important interactions such as *Hydrastis canadensis* and *Hypericum perforatum* (Roby CA, Et al.2000). Taking into account the distribution and use of the *Hypericum perforatum* in our country, it is important that such information is made clear to the patient in advance, when the doctor prescribes a preparation that can interact with this plant or others with similar effect to it. Interaction risks are primarily based on major CYP enzymes (cytochrome P450). Herbal dietary supplements from *Hypericum perforatum* are categorized as high risk of drug interactions. It can reduce effectiveness of cyclosporine, tacrolimus, warfarin, protease inhibitors, irinotecan, theophylline, digoxin, etc. (Roby CA, Et al.2000).

One of the most important reasons for undertaking this study and distribution of the questionnaire on the knowledge that people have about the interaction of drugs and food supplements or herbal products, was the mass use of supplements and herbal products in the same time. Usually, people consider food supplements safe to use and they are unaware of possible adverse effects associated to their usage. Using food supplements, herbal products and other natural products in a combination with different drugs may lead not only to adverse reactions deriving from an incorrect use, but it can cause also different types of interactions between these compounds.

Table 5. Source of information regarding drug-supplements interactions

| Frequency | Source of information |
|-----------|---|
| (48%) | From the internet/social media |
| (34%) | From the pharmacist |
| (18%) | From the doctor |
| (12%) | From the doctor, fitness coach/nutritionist |

Regarding the source of information, patients have on drug-supplement interaction, most of them receive this information from the internet/social media or supplements leaflet (48%),

from the pharmacist (34%), from the doctor (18%) and 12% had this information from the doctor and fitness coach or nutritionist (this 12% is included in the group of 135 individuals that have this information from the doctor) (Fig. 3).

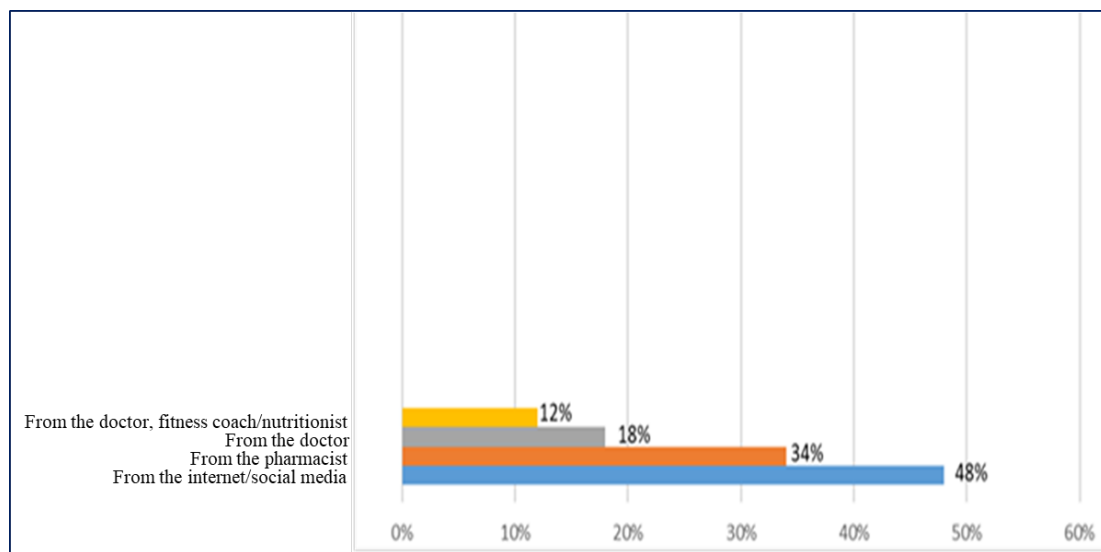


Figure 4. Source of information regarding drug-supplements interactions

In support of this survey, we also analyzed a wide group of individuals tested for the amount of vitamin D in circulation, in order to see any possible effect of taking supplements regularly on biochemical markers in our body. Vitamin D level was measured in a group of 2295 randomly chosen individuals, presented in the laboratory for routine analysis. Compared to the data from previous studies during the period from 2009-2010, where a mean value of 21.49 (\pm 7.6) ng/ml (Rumano, M., Et a. 2021) for vitamin D was observed, there is a slight increase in vitamin D concentration from 2019-2022, with a mean value of 24.14 (\pm 9.07) ng/ml. Regardless the extra care and supplements intake, the range varies from 5.8-125.6 ng/ml and the level of vitamin D insufficiency (72 %) is still high in the population. Although the long time use of vitamin D supplements or high daily doses sometimes (4000-5000 IU), no cases of hypercalcemia were observed in this group.

Regarding the vitamin D level, we have observed an increase of about 3% higher than ten years ago. Although we observe this change, still there is a high level of vitamin D insufficiency in population (about 72%). This increase can be linked to the increase of vitamin D intake during pandemic time, because people were more aware about the importance of a healthy diet, food supplements and vitamins in particular.

Table 6. Vitamin D data from 2019-2021 compared with the data from 2009-2010

| Gender | % | Vitamin D (ng/ml) 2009-2010 | Vitamin D (ng/ml) 2019-2021 | Minimum (ng/ml) | Maximum (ng/ml) |
|--------|------|-----------------------------|-----------------------------|-----------------|-----------------|
| F | 72.2 | 20.89 | 23.66 | 5.8 | 125.6 |
| M | 27.8 | 22.49 | 25.4 | 8.1 | 80.7 |

According to the most recent studies, vitamin D is proven to have a significant impact in infectious diseases. The role of vitamin D is now expanded and recent studies have proven and identified the effects of vitamin D on the immune system. Until now, the role of vitamin D as a determinant in mineral metabolism was well known and it was linked to mineral metabolism and rachitic bone diseases or osteoporosis.

This is a fat soluble vitamin that is obtained mainly through the sunshine (80 %) or via the diet (20 %) in the form of ergocalciferol from plants and cholecalciferol from animal products. The serum levels of vitamin D are influenced by many factors: age, gender, race, obesity, diet, malabsorption, season, geographical latitude and altitude. The low vitamin D status is, to a large extent, caused by dysregulation of vitamin D metabolism as a result of renal insufficiency or liver issues too. Vitamin D deficiency has also been identified as a worldwide public health issue that is associated with an increase in the prevalence of related-chronic diseases.

Vitamin D intake benefits, stimulates people to use more supplements, without considering the adverse effects, the possibility of toxicity due to the high amount of vitamin D present or the buildup of calcium in our blood causing hypercalcemia.

Taking into account the attention given to the use of vitamins and microelements during the pandemic period, almost 90% of people say that being informed about drug-supplements interactions is very important and crucial for their health. Although they are exposed to a lot of information, they consider it insufficient and sometimes not trustful. Other studies mention that supplements continue to be used by an increasing proportion of the population, so their contribution to diet, health and disease needs to be monitored (Lentjes MAH. 2019).

Conclusion

As a conclusion we can say that using food supplements, herbal products and other natural products in a combination with different drugs may lead not only to adverse reactions deriving from an incorrect use, but it can cause also different types of interactions between these compounds.

Pharmacists recommend taking medications and supplements at least an hour apart and to keep a diary about any side effects that come on long with supplements use. It is important to avoid using supplements that contain large amounts of ingredients too.

Acknowledgements or Notes

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