

# Effects And Side Effects Of Fruit-, Vegetable- And Berry-Powder In Case Of Juiceplus+®

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## Abstract

In daily challenge of job, stress and private life, nutrition is of growing importance. Hecticness of daily routine gives people insufficient time for well-balanced nutrition and balanced intake of fruits and vegetables. So for people it appears reasonable to use nutrition supplements as compensation for feared malnutrition. There is a tremendous variety of products, confusing for consumers. When patients ask their doctors for advice whether to take or not to take nutrition supplements and want to get tips for better well-being and prophylaxis, the recommendations like more exercise and healthy nutrition are inconvenient, difficult to implement, and often not feasible. The ingestion of nutrition supplements seems to be easier, and better than doing nothing. This might be, because physicians know too little about nutrition supplements, especially about effects, side effects and ingredients. For most of the nutrition supplements the scientific knowledge is bad, the knowledge of physicians is worse, and the attention to nutrition supplements is worst. In about 50 percent of patient contacts, physicians do not ask the patient for supportive ingestions, which would be the very least, especially in the fact, that about 80 per cent of people state to use nutrition supplements.

Browsing the scientific databases shows only few peer - reviewed scientific publications about over-the-counter preparations. One of the American market leaders in nutrition supplements, the National Safety Associates GmbH (NSA) with its product line JuicePlus+®, is one of few companies offering nutrition supplements and being engaged in scientific assessment of these products.

In conclusion: The nutrition supplement JuicePlus+® by NSA is one of the best investigated food concentrates worldwide, no other preparation is able to show these number of Pubmed listed publications. There are reports about beneficial effects and potential side-effects. There is a risk of overdosage of some ingredients like Vitamin E,  $\beta$ - carotin, Vitamin C and folic acid in order to guidelines of the German Society of Nutrition. Our aim is not to present new studies but to present the actual data basis of JuicePlus+®. We see an essential need for independent double-blind randomized crossover studies concerning effects and side-effects of JuicePlus+® in healthy volunteers and/or patients with defined medical conditions.

## INTRODUCTION

In the last decades the market of nutrition and dietary supplements grew up significantly. An analysis of IMS Health shows a volume of 911,1 million euros for over the counter vitamins, minerals and nutrition supplements in 2011.<sup>14</sup> The difference of 4,6 million euros more versus 2010 is notable.<sup>1</sup> Especially middle-aged people are bothered by the fear of malnutrition.<sup>29</sup> To resort to nutrition supplements seems natural. The formula sounds quite simple: doing yourself good daily just with low effort and some capsules, powder or tablets; avoid supposed deficiencies and balance missing fruit-and vegetable consumption – without stress, without intensive physical training and without conquering the personal lack of drive.

There is a not even a remotely comprehensible number of substances and combinations of substances to be sold as nutrition supplements. Exact numbers of sales quantity are rare, because most of the products are sold over the world wide web, franchise - or multi – level –marketing - systems. Practical numbers of sale and volume of sale don't get published and in case of publication confirmationis quite complicated.

Added, it is not transparent, which company rules a series of nutrition supplements at the first look. For example the preparations Centrum® and VitasprintB12® are part of the Pfizer Health Care GmbH (Pfizer Health Care GmbH, Centrum®, VitasprintB12®, Berlin, Germany)<sup>6,45</sup> and Supradyn®, Redoxon®, One-a-day®, Berocca® and Elevit®

belong to BayerHealthCare AG (BayerHealthCare AG, Supradyn®, Redoxon®, One-a-day®, Berocca®, Elevit®, Leverkusen, Germany).<sup>3</sup>

Mostly consumer don't know that nutrition supplements do subject to marginal statutory provisions only and do not need statutory tests series like drugs before their successful admission. The German edict of dietary supplements provide just a rough framework and specifies the permitted substances mainly.<sup>19</sup> The edict contains no specific recommendation or regulation of maximum admissible concentrations of admitted substances.

Scientific papers about individual commercial preparations are quite rare. Despite this there are indications on effectiveness, in part over side-effect reports. Producers and distributors of dietary supplements are very successful to accomplish the consumers respectively patients in many cases much better than the academic medicine.

In this review we respond to the question: how much do we know about effects and side – effects of food concentrates marketed as dietary supplement, using the example of JuicePlus+® (National Safety Associates GmbH, Juice Plus+®, Basel, Switzerland) by National Safety Associates GmbH (NSA). We choose Juice Plus+®, because despite the slender there are scientific papers published in peer - reviewed journals concerning JuicePlus+®.

### METHODS

We searched for scientific papers at Pub Med and Medline Databases with following key words „encapsulated fruit and vegetable powder“, „vegetable powder“, „fruit powder“, „berry powder“, „juice plus supplement“, „juice plus“ and „juice plus capsules“. The product web page of Juice Plus+® was screened for relevant informations.<sup>10</sup> Beside Pubmed and Medline we scanned the reference lists of the Pubmed /Medline listed publications for relevant material. Added we start a detailed search via appropriate publicly available search machines like Google and Yahoo.<sup>12,50</sup> The criteria for scientific papers were original publications, letter to the editor, clinical communication to the editor, abstracts, reviews or poster presentations. A sum of 33 scientific papers and many pieces of material, which did not accord to the criteria above, was collected until June 2013. The original publications were examined from the following points of view: subjects, criteria of ex - and inclusion, study design, aim of study, preparation and taking schedule, sponsors, connection to the company NSA, results und specifics. To get an idea of the scientific quality rating we

analyzed the actual impact factors and the impact factors of the year of publication of the journals, published in. For a rough idea of the use of nutrition supplements in the personal surrounding we created a questionnaire. The questionnaire asked for initials, age, profession, the use of nutrition supplements, which nutrition supplement exactly, the expectances of use and whether the use is declared in a medical drug anamnesis (for details see<sup>5</sup>).

The original plan to analyze the effect of JuicePlus+® related to different disease patterns was unrealizable because of lack of resilient data.

### RESULTS

#### Analysis of publications

JuicePlus+® is an encapsulated fruit-, vegetable –and berry powder concentrate. The company National Alternatives International (NAI) product the preparation, NSA is the distributor. There are three different powder-compositions: JuicePlus+® Orchard and Garden Blend are composed of 17 different fruits, vegetables and grains and JuicePlus+® Vineyard Blend of 9 different berries, as the manufacturer names.<sup>18</sup> Referred to manufacture's information JuicePlus+® Orchard and Garden Blend is a composition of apple, orange, pineapple, cranberry, peach, acerola cherry, papaya, carrot, parsley, beet, kale, broccoli, cabbage, spinach, tomato, oat bran, brown rice bran; JuicePlus+® Vineyard Blend a composition of concord grape, blueberry, cranberry, blackberry, bilberry, raspberry, red currant, black current and elderberry. <sup>18</sup> Which exact proportions of the different fruits, vegetables and berries are used, is not public.

The 33 publications were composed of 25 original papers, 2 reviews, 1 letter to the editor, 2 posters, 1 clinical communication to the editor, 1 book chapter and 1 abstract. On looking through the papers the multitude of different topics attracted attention (see table 1).

Altogether there are many auspicious approaches for a comprehensive research. One complexity of the scientific comparability is the missing consistency of the study preparation: A comparison of the different ingredients, used in the studies, showed multiple combinations of fruits, vegetables and berries (for more details see 5). Beside this fact Vitamin E, ascorbic acid, folic acid and β - carotene are admixed through the company to provide firm concentrations.<sup>17</sup>

In relation to the whole published material a little number of

researcher and research groups were publishing about JuicePlus+®. 16 authors of 8 research groups released 18 publications, complying 54.54% of 33 publications.<sup>5</sup> Wise and Lamprecht were involved in 12 papers, complying 36.36% of 33 publications. 5 Both authors have or had economical connections with JuicePlus+®: Wise was employed at NSA and NAI and stockholder of NSA until his death in 2011.<sup>15</sup> According to Lamprecht’s Xing profile he got 96.320,89 ¥ aid money between 2005 – 2006<sup>49</sup> and was member of the Roadtour of JuicePlus+®, a promotion tour of the “Intelligent weight management program” of JuicePlus+® Shape.

Many authors are connected with NSA or NAI, in part they are distributor or recommend JuicePlus+®. In not all publications these connections are declared properly.<sup>5</sup> It is not reproducible whether the connection with the companies existed before, during or after the scientific study on JuicePlus+®.

There exist a few reports of side effects in connection with JuicePlus+®. Naing et al. reported the case of a 51 years old woman with endometrium carcinoma, who came to plan a therapeutic medical procedere.<sup>31</sup> Initial blood parameters were in normal rage, the follow up blood analysis showed elevated total bilirubin, aspartate aminotransferase, and alanine aminotransferase.<sup>31</sup> The changed blood panel accompanied with scleral jaundice and slight abdominal pressure pain.<sup>31</sup> Neither medication nor eating habit were changed recently, the long-term medication was taken dependably. 31 Since a short time the patient declared the regular use of JuicePlus+®.<sup>31</sup> Ultrasound, CAT scan and serological tests gave no evidence for intra- or extrahepatic obstruction, hepatomegaly or liver metastases. 31 The liver biopsy showed no carcinoma, but focal hepatocellular degenerative changes and steatosis with mild sinusoidal dilatation against a background of mild cholestasis, minimal lobular and portal acute and chronic inflammation were findings most consistent with a drug effect. 31 After giving up the use of JuicePlus+® the blood parameters and the general condition normalized. 31 Whether the effects came from JuicePlus+® only or from an interaction between the long-term medication and JuicePlus+® could not be clarified. 31

The Memorial Sloan- Kettering Cancer Center, New York, USA advises attention in the usage of JuicePlus+®, because of possible interactions with chemotherapy. 30 The efficacy of certain chemotherapeutics was discussed to be possibly restrained, because of the reduction of free radicals which

are needed for proper cytotoxic effects. 30 Houston et al. consider a correlation between the use of JuicePlus+® and gastrointestinal distress.<sup>13</sup> 2 subjects reported on hive-like rash the study panel of Inserra et al.<sup>15</sup>

These reports of possible side effects document the effect of the preparation JuicePlus+®, and the need of differentiated scientific investigation.

**Table 1**

Topics of publications about JuicePlus+® (Because of clear arrangement the first author is termed only, for details please see reference list)

Topic	Publication
JuicePlus+® and adiposity	Wise 2009 <sup>47</sup>
	Wise 1996 <sup>48</sup>
	Leeds 2000 <sup>28</sup>
	Panunzio 2003 <sup>36</sup>
	Samman 2003 <sup>39</sup>
	Watzl 2003 <sup>46</sup>
	Kiefer 2004 <sup>21</sup>
JuicePlus+® and biochemistry	Lamprecht 2005 <sup>23</sup>
	Bamonti 2006 <sup>2</sup>
	Bloomer 2006 <sup>4</sup>
	Goldfarb 2007 <sup>11</sup>
	Kawashima 2007 <sup>20</sup>
	Lamprecht 2009 <sup>25</sup>
	Novembrino 2011 <sup>33</sup>
JuicePlus+® and common cold	Roll 2011 <sup>38</sup>
JuicePlus+® and vasculature	Plotnick 2003 <sup>37</sup>
	Schwartz 2006 <sup>41</sup>
JuicePlus+® and skin	De Spirt 2012 <sup>8</sup>
	Lamprecht 2012 <sup>27</sup>
JuicePlus+® and hypertension	Houston 2007 <sup>13</sup>
JuicePlus+® and immunology	Inserra 1999 <sup>15</sup>
	Smith 1999 <sup>43</sup>
	Lamprecht 2007 <sup>24</sup>
	Nantz 2006 <sup>32</sup>
	Jin 2010 <sup>16</sup>
	Lamprecht 2010 <sup>26</sup>
Naing 2010 <sup>31</sup>	
JuicePlus+® and the metabolic syndrom	Ali 2011 <sup>1</sup>
JuicePlus+® and the function of muscles	Goldfarb 2011 <sup>10</sup>
JuicePlus+® and periodontosis	Chapple 2012 <sup>7</sup>
JuicePlus+® in reviews	Lamprecht 2009 <sup>25</sup>
	Esfahani 2011 <sup>9</sup>
JuicePlus+® and gravidity	Odom 2006 <sup>34</sup>

**Results of questionnaire**

We did the survey to get a rough idea of the use of nutrition supplements in our personal surrounding. It is a random sample and does not pretend to have universal validity. We distributed the questionnaire between March 2012 and April 2012.

The questionnaire requested the following items:

- Initials, actual age, gender and professional confession
- Did you ever use over the counter products like proteins, minerals, protein shakes, multi – vitamin - preparations, vitamins, sportdrinks or anything similar?(yes/no)
- If the answer is „no“, we thank you for participation
- If the answer is „yes“: which expectations did you have on this preparation?
- Did the preparation deliver your expectations?(yes/no)
- Did you tell your doctor about using this preparations?(yes/no)

We had a recirculation of 175 questionnaires (for complete raw data we refer to 5 ). 101 men and 74 women with average age of 43.23 years took part. Only 36 participants (20.57 %) never used nutrition supplements, minerals or special diets. 5 In the midst of the user of nutrition supplements we found notable more men (81 subjects, 58.27%). 5 For 90 subjects (64.75 %) the expectations were confirmed. 5 29 (20.86 %) did not find their expectations fulfilled and 10 subjects (7.19 %) did not express themselves. 67 subjects (48.20%) told their doctor about the usage of nutrition supplements in the drug anamnesis, the others did not. 5

An analysis whether there were taken one or multiple preparations revealed the following: Based on 139 participants using such substances 42 (30.22%) earned one preparation only (inclusive single multi - vitamin preparations); 97(69.78%) earned minimum 2 preparations or more. 10 Range was between 2 and 7 different preparations. 5

Relating to different preparations there only was a limited systematic combination possible, because of a lack of correct statements. 5 All in all 100 different substances or substance - combinations were referred. 5 With 48 nominations magnesium was the front- runner followed by JuicePlus+®, JuicePlus+®, Vitamin C (40 nominations), zinc (16 nominations), calcium (15 nominations) and proteindrinks (14 nominations). 5

We did not inquired for drugs nevertheless people mentioned drugs like acetylsalicylic acid and iron preparations in the same breath with nutrition supplements. 5

### CONCLUSIONS

The interest in nutrition and the consciousness for individual

responsibility of oneself health grows notable since the last decades. From medical point of view the development is appreciated particularly in terms of prevention. The idea in doing you and your health good must be supported forcefully. Since long time nutrition is an important starting - point for better health and well - being. NSA and NAI are companies who lead the way of the scientific discovery of nutrition supplements: both try to acquire information about their products and to provide the scientific community with this knowledge. However the results of the published material all in all are weak: on the one hand because of the many different worked topics, which represent only small aspects, on the other hand because of various study designs and variable test preparation. JuicePlus+® has detectable effects like elevated concentrations of carotenoids<sup>7,8,13,15,20,28,32,39,43,46,47</sup>, ascorbic acid<sup>28,39,21,4,15,11,32,16</sup>, Vitamin E<sup>28,39,21,4,11,8,13,15,32,16</sup> and folate<sup>13,20,21,36,39</sup>. The question about potential of rather high daily dose rates of different ingredients like Vitamin E or carotenoids must keep at the focus in relation to science - based references of the nutrition associations. The good old phrase „more is always better“ does not apply in each and every case; too high daily dosages can cause relevant damage: Törnwall et al. reported in their ATBC – study about a significantly higher risk of mortality at the use of supplemented 50 mg (ca. 74.6 international units (IU)) Vitamin E and 20 mg  $\beta$  - carotene daily over 6 years in smokers.<sup>44</sup> 2011 Klein et al. published their „selenium and Vitamin E cancer prevention trail“ (SELECT- study), the results showed an elevated cardiac risk and a clear elevated risk of prostate cancer with 400 IU (ca.268.46 mg) Vitamin E daily.<sup>22</sup> A significant elevated incidence of lung cancer was described of Omenn et al. 1996 in connection with the use of 30 mg  $\beta$  - carotene and 25,000 IU retinol daily.<sup>35</sup> The results were confirmed by Satia et al. with different dosages of  $\beta$  - carotene.<sup>40</sup> In addition pharmacological interactions cannot be excluded completely, how you can see at the case report of Naing et al.<sup>31</sup> and the recommendations of the Memorial Sloan-Kettering Cancer Center, New York.<sup>30</sup> It has to be considered, that many users refer to subjective clear better well - being and the feeling of better health.<sup>31</sup> In times of tight financial conditions people spend great amounts in such preparations monthly. For example: The price of JuicePlus+® Vineyard -, Orchard - and Garden Blend are 67.50 \$ or 75.50  $\square$  monthly.<sup>42,18</sup> A placebo-effect is implausible, and the user group of nutrition supplements is large.

There is a need for proper scientific research of JuicePlus+® and similar preparations, because the substances are highly

effective. For a differentiated assessment and to figure out potential benefits at special disease patterns large independent placebo controlled studies should be done. For comparable data it must be the same preparation with exact declaration of fruits, vegetables and berries and their portions as well as exact data about percentage of admixed Vitamin E,  $\beta$  – carotene, ascorbic acid and folate. In conclusion we point out that all results and reports refer to the product JuicePlus+® only and the statements are not valid

for other preparations.

## **DISCLOSURE**

All authors report no conflicts of interest in this study, especially there is no economic or other cooperation with NSA and partners. All authors also do not have any connections to any other network marketing company.

## **References**

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