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Hidden sodium in effervescent-tablet dietary supplements and over-the-counter drugs: a comparative cross-sectional study

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ABSTRACT

Objective Dietary sodium intake represents a risk factor for cardiovascular disease and mortality. The study sought to analyse the sodium content of effervescent dietary supplements and drugs in Germany and the USA.

Design Comparative cross-sectional study.

Setting and methods The sodium content of 39 dietary supplement effervescent tablets available in Germany was measured in May and June 2022 using optical emission spectrometry with inductively coupled argon plasma. The sodium content of 33 common pharmacy-only effervescent tablets (over-the-counter (OTC) drugs) in Germany was obtained from the summary of product characteristics. We compared the sodium content of the measured German dietary supplement effervescent tablets to that of 51 dietary supplement effervescent tablets available in the USA (data: National Institutes of Health's Dietary Supplement Label Database).

Results The measured sodium content in the German dietary supplements was 283.9±122.6 mg sodium/tablet, equivalent to 14±6% of the maximum recommended daily sodium intake (MRDSI). Vitamin products had the highest (378.3±112.8 mg, 19±6% of MRDSI), and calcium products had the lowest mean sodium content (170.4±113.2 mg, 9±6% of MRDSI). Vitamin products contained significantly more sodium than magnesium (378.3 mg vs 232.7 mg; p=0.004), calcium (378.3 mg vs 170.4 mg; p=0.006) and mineral products (378.3 mg vs 191.6 mg; p=0.048). The sodium content measured in products available in Germany was higher when compared with the declared sodium content on the label of the products sold in the USA (283.9 mg vs 190.0 mg; p<0.001). The median summary of product characteristics-declared sodium content of a single dose of the German OTC drugs was 157.0 mg (IQR: 98.9–417.3 mg); pain/common cold drugs contained the most sodium (median: 452.1 mg; IQR: 351.3–474.0 mg).

Conclusion Effervescent tablets of nutritional supplements and OTC drugs contain high amounts of sodium, which often is not disclosed.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The measurement of sodium content in dietary supplement and pharmacy-only effervescent tablets gives detailed insights into the quantities of hidden sodium in these dosage forms.
⇒ We provide sales figures for effervescent tablets sold in German pharmacies.
⇒ However, data for the quantities sold of dietary supplement effervescent tablets from discounters, grocery stores and drugstores are not publicly available.
⇒ The association between the ingestion of effervescent tablets and cardiovascular outcomes was not investigated.

INTRODUCTION

Dietary sodium intake is associated with elevated blood pressure (BP), increased cardiovascular events including stroke and death from any cause.[1–5] In patients with arterial hypertension, the long-term reduction of 1800 mg less sodium/day (this corresponds to 4600 mg table salt/day) was associated with a reduction in systolic/diastolic BP of 5.1/2.7 mm Hg.[4] The extent of the sodium restriction was proportional to the reduction in BP, with a more pronounced effect in patients with hypertension.[6] Even modest reductions in dietary sodium have been shown to reduce cardiovascular events, including myocardial infarction and stroke.[1 7] Dietary sodium consumption is an important risk factor for premature death and disability-adjusted life-years globally.[7] The WHO recommends reducing sodium intake to <2000 mg/day in adults, which is equivalent to 5000 mg of table salt (sodium chloride).[8] However, only a small proportion of the population achieves this goal.[9] The daily amount of table salt consumed is often much higher (9000–12 000 mg/day; 3500–7700 mg sodium/day), which may, in part, relate to hidden sodium consumption.[9 10]

Effervescent tablets often contain a relatively high amount of sodium in form of

sodium bicarbonate, sodium carbonate or sodium citrate and are frequently consumed without awareness of their sodium content.[11 12] This may be particularly relevant for dietary supplements and over-the-counter (OTC) effervescent tablets (eg, vitamin C, magnesium or analgesics) from groceries, drugstores, discounter and pharmacies because many manufacturers do not provide information on sodium content on the label. The present study sought to provide information about the often not labelled sodium content of dietary supplement effervescent tablets from large groceries and drugstores and sodium-containing effervescent tablets used as drugs from pharmacies. Country-specific differences in sodium content (products from Germany vs products from the USA) were set forth.

METHODS

Study design

A comparative cross-sectional study was conducted in 2022 and 2023 to examine and compare the sodium content of different categories of effervescent tablets.

Classification, place of purchase and analyses of dietary supplements available in Germany

The sodium content of 39 different dietary supplement effervescent tablets available in Germany (divided into the categories vitamins, magnesium, calcium, minerals and other products) from 11 manufacturers and 5 distributors was analysed in May and June 2022. The effervescent tablets were divided into categories based on the main active ingredient (eg, if a product mainly contains magnesium and only a little calcium related to the recommended daily dose, then it is assigned to the category magnesium). The products were purchased from two discounters (ALDI SÜD GmbH & Co. and Netto Marken-Discount Stiftung & Co. KG), one grocery store (Edeka Stiftung & Co. KG) and two drugstores (DM drogerie markt GmbH & Co. KG and Müller Handels GmbH & Co. KG) in Germany and then delivered to the laboratory unopened.

The analyses were performed by an accredited chemical laboratory in Germany (CBA GmbH, Kirkel-Limbach, Germany, Deutsche Akkreditierungsstelle D-PL-14360-01-00). After appropriate standardised sample preparation, optical emission spectrometry with inductively coupled argon plasma (ICP-OES) was used for analysis. The sample preparation (pressure digestion in Teflon-pressure-vessels with microwave-assisted heating) proceeded as follows. The effervescent tablets were ground up and a sample amount corresponding to the expected sodium content was weighed out exactly. This amount of powder was displaced first with 1 mL water and then with 3 mL 65% nitric acid and transferred to the Teflon-pressure-vessel. The digestion took place at 180°C in the digestion apparatus (microwave digestion system, CEM) for at least 20 min, followed by a cooling period. The vessels were filled up with water again to the nominal volume. Reference solutions and blank values were treated in the same way. After sample preparation, the solutions were transferred directly into the ICP-OES equipment (ICP-OES iCAP 6300 Duo, Thermo Fisher Scientific). All digestion and reference solutions were sprayed into an argon plasma, followed by selective detection of sodium emission radiation at 589.59 nm.

Classification and data source for over-the-counter drugs

The sodium content of 33 commonly sold pharmacy-only effervescent tablets (30 OTC and 3 prescription drugs, all referred to as 'OTC drugs' for convenience) from German pharmacies was derived from the respective package inserts or summary of product characteristics. The drugs were divided into the categories pain/common cold, cough, calcium/vitamin D and other drugs based on the main active ingredient. The analysis was based on data from the German Institute for Drug Use Evaluation (Deutsches Arzneiprüfungsinstitut e.V. (DAPI)). This database contains anonymised dispensing data from more than 95% of the community pharmacies in all 16 German federal states, claimed at the expense of the statutory health insurance (SHI) funds and a DataWare House to identify every product by a specific code ('Pharmazentralnummer', PZN). The SHI system, consisting of nearly 100 funds, covers 88% of the population, that is, approximately 73.3 million people. As the unit for prescribed drugs, we used defined daily doses (DDD)—that is, the assumed average maintenance dose per day for a drug used for its main indication in adults. Further, we analysed the aggregate amount of dispensed packages of drugs and diet supplements as effervescent tablets in community pharmacies and via mail-order using dispensing data reimbursed by SHI funds as well as private health insurance companies and OTC sales from the INSIGHT Health (https://www.insight-health.de/) and DatamedIQ (https://www.datamediq.com/) databases, respectively. Usual package sizes of pain/common cold and cough effervescent tablets are 10 or 20, of calcium/vitamin D 20, 40 or 100 tablets. The sodium content of the maximum recommended daily dose was also specified and confirmed by the data in the package insert and/or summary of products characteristics.

Classification and data source of dietary supplements available in the USA

The sodium content of 51 dietary supplement effervescent tablets available in the USA was derived in May 2023 from the Dietary Supplement Label Database. The National Institutes of Health's Dietary Supplement Label Database includes 156 957 current and historical label information from products marketed in the USA. Effervescent tablets with specified sodium content in the product information were included. The products were divided into the following categories based on the main active ingredient: vitamin, mineral, energy and other products.

Statistical methods

The data are presented as means±SD, medians and IQR or numbers (%). Normal distribution was tested using Kolmogorov-Smirnov/Shapiro-Wilk test and using a histogram. Analysis of variance (ANOVA) was used (after tested for all assumptions for ANOVA: normally distribution, independence of cases, homogeneity of variance) for comparisons of normally distributed parameters, and for comparisons between non-normally distributed parameters, the Kruskal-Wallis test was used. If these tests were significant, we used a post hoc method (Dunn-Bonferroni) for pairwise comparisons. For comparisons between two non-normally distributed parameters, the Mann-Whitney U test was used. A two-sided p value<0.05 was considered statistically significant. Statistical analyses were performed with SPSS (V.27.0.1.0).

Patient and public involvement

None.

RESULTS

Dietary supplement effervescent tablets in Germany

Online supplemental table 1 provides an overview of the included dietary supplement effervescent tablets available in Germany. The median weight of one tablet was 5.5 g, and the price ranged from €2.3 to €39.9 cents/tablet (median price/tablet: €3.2 cents). The sodium content of the effervescent tablets measured by ICP-OES is listed in table 1. On average, one effervescent tablet contained 283.9±122.6 mg sodium (table 2A). Vitamin products had the highest (378.3±112.8 mg) and calcium products (170.4±113.2 mg) the lowest mean sodium content. Vitamin products contained significantly more sodium than magnesium (p=0.004), calcium (p=0.006) and mineral (p=0.048) products (figure 1). Based on the recommended maximum intake of 2000 mg sodium/day, a single effervescent tablet contained as much as 4–28% of the maximum recommended daily sodium intake. The lowest sodium content/effervescent tablet was 76 mg (Magnesium 400, Fit+Vital), and the highest was 564.7 mg (Vitamin C 1000, Fit+Vital). The median sodium content was 5.1 g/100 g effervescent tablets, with the highest being 9.63 g sodium/100 g (Eisen+Vitamin C, Fit+Vital). Online supplemental figure 1 depicts the number of effervescent tablets according to sodium content (in 100 mg increments) grouped per category. One of 10 (10.3%) products contained more than 500 mg sodium/tablet. Only 5 (12.8%) products (all of the Mivolis brand) declared the sodium content on the packaging which was nearly identical to the measured sodium content.

Dietary supplement effervescent tablets in the USA

The sodium content of the various effervescent tablets is listed in online supplemental table 2. Among all screened products (n=981), only few declared the sodium content on the label (5.2%), allowing 51 products to be included. The median sodium content of a single effervescent tablet was 190.0 mg (IQR: 100–250 mg; table 2B) and no difference in sodium content between the various categories was found (p=0.061). A single effervescent tablet contained 2–18% of the maximum recommended daily sodium content. The measured sodium content of dietary supplements available in Germany was higher when compared with the declared sodium content of products available in the USA (p<0.001).

Pharmacy-only effervescent tablets

The sodium content declared on the summary of product characteristics of the OTC drugs sold in Germany is listed in table 3. The median reported sodium content of a single effervescent tablet was 157.0 mg (IQR: 98.9–417.3 mg; table 2C). The percentage of sodium consumed per effervescent tablet in relation to the maximum recommended daily sodium intake ranged from 3% to 29%. Pain/common cold drugs had the highest median sodium content (452.1 mg; IQR: 351.3–474.0 mg) and calcium/vitamin D drugs the lowest (87.0 mg; IQR: 52.0–103.0 mg). A single pain/common cold effervescent tablet contained significantly more sodium than one calcium/vitamin D effervescent tablet (p<0.0001). Online supplemental figure 2 depicts the number of effervescent tablets according to sodium content (in 100 mg increments) grouped per category. The median sodium content of the recommended daily dose of all included drugs was 384.0 mg (IQR: 139.0–1295.5 mg; table 2D) and for pain/common cold drugs 2776.5 mg (IQR: 1299.8–3333.0 mg), representing 19%/139% of maximum recommended daily sodium intake, respectively. The intake of eight tablets (maximum recommended daily dose) of Alka-Seltzer classic (aspirin, Bayer) would lead to the ingestion of 3560 mg sodium (figure 2), which encompasses 178% of the maximum recommended daily sodium intake. The sodium content of the maximum daily dose of pain/common cold drugs was significantly higher than the sodium content of the maximum daily dose of calcium/vitamin D drugs (p<0.0001) and cough drugs (p=0.007). No significant difference in sodium content between the dietary supplement calcium effervescent tablets and the pharmacy-only calcium/vitamin D effervescent tablets was seen (p=0.109).

Online supplemental figure 3 summarises the main results.

DISCUSSION

This study assessed the sodium content of nutritional supplement effervescent tablets available in Germany and found the sodium amount to range from 76.0 mg/tablet to 564.7 mg/tablet (average 283.9 mg/tablet) representing up to 28% of the maximum recommended daily sodium intake. Vitamin products contained more sodium than magnesium, calcium and mineral products. The sodium amount/tablet of OTC drugs ranged from 52 mg to 575 mg (median 157.0 mg) representing up to 29% of the maximum recommended daily sodium intake. The intake of the recommended daily dose of one OTC drug would

Table 1 Sodium content of German dietary supplement effervescent tablets

Category	Brand name	Sodium content/tablet (mg)	% of maximum recommended daily sodium intake*	Sodium (g)/100 g product	Weight/ tablet (g)
Vitamins	fit+Vital Vitamin C1000	564.70	28	9.01	6.27
	elkos Vivede Vitamin C+Zink, Selen, und Vitamin D3	541.10	27	8.95	6.05
	Doppelherz aktiv Vitamin C+Zink	512.80	26	8.11	6.32
	ProLife Vitamin C+Zink, Selen, Vitamin D3	507.90	25	8.48	5.99
	Doppelherz aktiv Vitamin D3 2000 I.E.	485.10	24	7.44	6.52
	SilaVit Vitamin B12	367.30	18	9.05	4.06
	Vitalis Vitamin C 120 mg	341.50	17	8.54	4.00
	Mivolis Vitamin B12	333.00	17	8.08	4.12
	Mivolis Vitamin C	330.30	17	8.02	4.12
	Doppelherz aktiv A-Z Multivitamin+Mineralien	321.40	16	5.10	6.30
	SilaVit Vitamin C	318.00	16	7.92	4.02
	fit+Vital Multivitamin	304.60	15	7.57	4.02
	elkos Vivede Multivitamin+Mineralstoffe	273.50	14	4.56	6.00
	ProLife Multivitamin+Mineralstoffe	263.20	13	4.38	6.01
	fit+Vital Multivitamin+Mineral	210.70	11	5.26	4.01
Magnesium	Doppelherz aktiv Magnesium 400	332.50	17	5.11	6.51
	Vitalis Magnesium 240 mg	306.10	15	5.58	5.49
	Abtei Magnesium 400 Plus Vitamin C+E	298.70	15	5.56	5.38
	Doppelherz aktiv Magnesium+Calcium+ D3	271.20	14	4.12	6.59
	Doppelherz aktiv Magnesium 500+B12	268.90	13	4.12	6.53
	Mivolis Magnesium	262.70	13	6.39	4.11
	elkos Vivede Magnesium+B-Komplex, Vitamin C und E	248.40	12	4.13	6.01
	Doppelherz aktiv Magnesium+Kalium Sport	245.50	12	3.72	6.60
	ProLife Magnesium+B-Komplex, Vitamin C&E	238.00	12	3.95	6.03
	Kneipp Magnesium+Calcium+ D3	221.30	11	4.91	4.51
	Abtei Magnesium+Kalium Aktiv Plus	138.10	7	2.52	5.48
	fit+Vital Magnesium	117.80	6	2.95	3.99
	fit+Vital Magnesium 400	76.00	4	1.40	5.41
Calcium	ProLife Calcium+Vitamin K1, D3, Folsäure	335.90	17	5.60	6.00
	Mivolis Calcium	145.90	7	3.53	4.14
	fit+Vital Calcium+D3	116.20	6	2.89	4.02
	fit+Vital Calcium 1000	83.70	4	1.36	6.17
Minerals	Kneipp Männer Mineralstoffe	217.00	11	3.87	5.61
	Kneipp Frauen Mineralstoffe	209.40	10	3.33	6.29
	Mivolis Multi-Mineral	148.40	7	3.62	4.10
Other products	fit+Vital Eisen+Vitamin C	382.90	19	9.63	3.98
	SilaVit Immun Aktiv	363.80	18	8.55	4.25
	sanotact Recovery+Aminosäuren	187.60	9	3.54	5.29
	isostar Hydrate & Perform	181.00	9	1.51	11.99

*Maximum recommended daily sodium intake according to WHO recommendations.[8]

Table 2 Sodium content per: (A) Dietary supplement effervescent tablet available in Germany, (B) dietary supplement effervescent tablet in the USA, (C) OTC effervescent tablet, (D) recommended daily dose of the included OTC effervescent tablets

(A) Category	Sodium content (mg)/tablet mean±SD	% of the maximum recommended daily sodium intake* mean±SD
…all included products	283.9±122.6	14±6
…vitamin products	378.3±112.8	19±6
…magnesium products	232.7±76.7	12±4
…calcium products	170.4±113.2	9±6
…mineral products	191.6±37.6	10±2
…other products	278.8±109.5	14±6
(B) Category	**Sodium content (mg)/tablet Median (IQR)**	**% of the maximum recommended daily sodium intake* Median (IQR)**
…all included products	190.0 (100.0–250.0)	10 (5–13)
…vitamin products	100.0 (72.5–230.0)	5 (4–12)
…mineral products	250.0 (140.0–360.0)	13 (7–18)
…energy products	190.0 (150.0–260.0)	10 (8–13)
…other products	210.0 (158.8–256.3)	11 (8–13)
(C) Category	**Sodium content (mg)/tablet Median (IQR)**	**% of the maximum recommended daily sodium intake* Median (IQR)**
…all included drugs	157.0 (98.9–417.3)	8 (5–21)
…pain/common cold	452.1 (351.3–474.0)	23 (18–24)
…cough	138.8 (112.8–157.9)	7 (6–8)
…calcium/vitamin D	87.0 (52.0–103.0)	4 (3–5)
…other drugs	267.0 (119.8–387.5)	13 (6–19)
(D) Category	**Sodium content (mg) of the maximum daily dose Median (IQR)**	**% of the maximum recommended daily sodium intake* Median (IQR)**
…all included drugs	384.0 (139.0–1295.5)	19 (7–65)
…pain/common cold	2776.5 (1299.8–3333.0)	139 (65–167)
…cough	297.0 (144.5–427.0)	15 (7–21)
…calcium/vitamin D	104.0 (96.3–104.8)	5 (5–5)
…other drugs	801.0 (312.8–1155.5)	40 (16–58)

*Maximum recommended daily sodium intake according to WHO recommendations.[8]
OTC, over-the-counter.

lead to a median consumption of 384.0 mg sodium, and as high as 2776.5 mg for pain/common cold drugs. The major differences in the product classes' sodium contents are probably due to the variable CO_2-dependent solubilities. More sodium bicarbonate and/or sodium citrate is required for poorly soluble active ingredients in effervescent tablets for them to dissolve quickly and completely in water. The large variations within individual product classes remain unexplained. Products available in the USA also contain a relevant amount of sodium (ranging from 40 mg to 360 mg/tablet). Of note, dietary supplement effervescent tablets available in Germany contained more measured sodium than that declared in those available in the USA. This may, in part, be related to selection bias since only a few manufactures from the USA voluntarily provide information about the sodium content.

Dietary sodium intake has been linked to serious harmful effects, including BP elevation and all-cause death.[1 3 4 13 14] The 2017 report of the Global Burden of Disease study listed excess sodium intake among the major dietary risks, estimated to cause 3 million deaths every year worldwide.[7] A recently published, randomised trial in 20 995 subjects showed that using a table salt substitute containing 75% sodium chloride and 25% potassium chloride (as opposed to regular table salt containing 100% sodium chloride) reduced stroke, cardiovascular events and death.[1] Consequently, the WHO recommends that daily sodium intake should not exceed 2000 mg.[8] Many national and international societies have advocated for actions to lower dietary sodium intake through public education, labelling of foods and improved formulations of convenience food. Nonetheless, the daily sodium intake around the

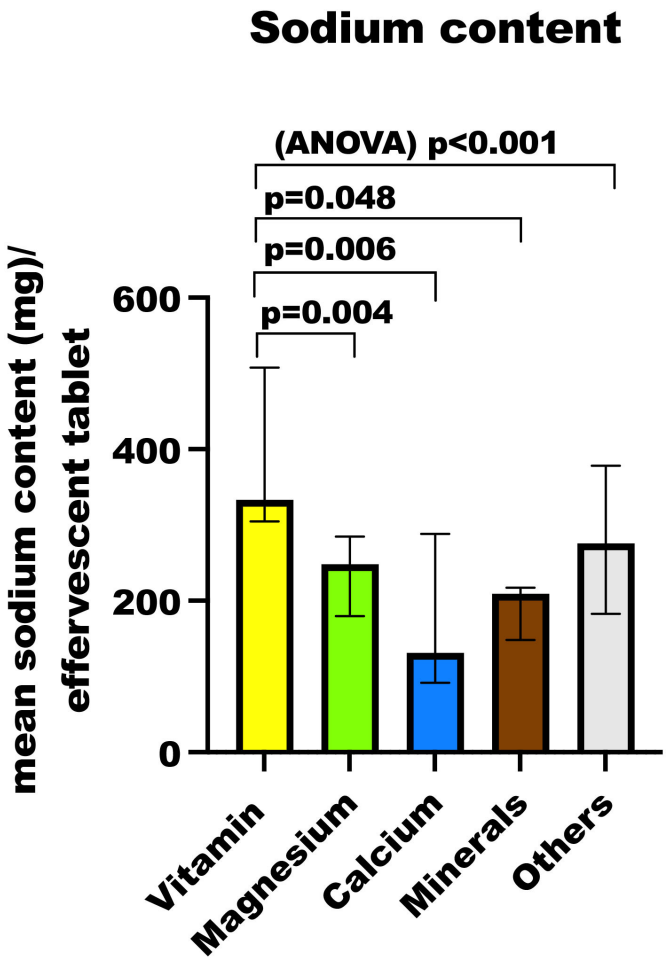

Figure 1 Mean sodium content of dietary supplement effervescent tablets available in Germany, by category. ANOVA, analysis of variance.

world is often much higher (9000–12 000 mg table salt/day; 3500–7700 mg sodium/day), which may, in part, be aggravated by hidden sodium consumption.[10 15]

For improved and quick solubility, effervescent tablets often contain high amounts of sodium[11] as sodium bicarbonate, sodium carbonate and/or sodium citrate. The impact of sodium-containing effervescent, mainly paracetamol (acetaminophen) tablets on BP, acute heart failure events and cardiovascular risk was investigated in several studies.[16–19] The intake of effervescent paracetamol tablets (with 545 mg sodium/dose) was shown to increase 24-hour systolic BP by 5.0 mm Hg.[17] Other trials showed an association between the intake of sodium-containing effervescent paracetamol tablets (390–440 mg of sodium/tablet) and an increased risk of hospitalisation for heart failure,[18] cardiovascular risk and all-cause mortality among patients with and without hypertension.[11 16 19] The mechanism by which the active substance paracetamol increases BP has not been conclusively clarified; inter alia an influence on the cyclooxygenase pathway is discussed.[20 21] Nevertheless, sodium containing paracetamol effervescent tablets deteriorate BP control mainly caused by the sodium in the effervescent tablets, as evident by the fact that after switching from paracetamol effervescent tablets to paracetamol tablets (without sodium), a decrease in BP was observed.[22]

This provides evidence that effervescent tablets increase sodium intake which might be associated with an increased risk for cardiovascular diseases.[1 3 4 13 14] A large case–control study comprising 1 292 337 patients with a mean follow-up of 7.2 years investigated the association between cardiovascular events and sodium-containing effervescent, dispersible and soluble drugs.[19] Participants were prescribed sodium-containing formulations or matched standard formulations of the same drug. A total of 61 072 patients with a cardiovascular event were matched with controls. The sodium-containing substances were largely painkillers or calcium drugs with a wide range of sodium content (4.6–427.8 mg/tablet).[19] The adjusted OR for exposure to sodium-containing drugs were 1.16 (95% CI: 1.12 to 1.21) for the composite of myocardial infarction, stroke or vascular death, 1.28 (95% CI: 1.23 to 1.33) for all-cause mortality and 7.18 (95% CI: 6.74 to 7.65) for hypertension.[19] Of note, the sodium content of some of the included effervescent tablets in this study is comparable with the sodium content of the drugs included in the mentioned study.[19]

The ancillary sodium intake through effervescent tablets is often neglected or unknown. Herein, the average sodium content of effervescent food supplements tablets in Germany was 283.9 mg/tablet, and the median sodium content of the pharmacy-only effervescent tablets was 157.0 mg/tablet. Consuming one of the included effervescent vitamin tablets or pain/common cold tablets corresponds to about one-fifth (19%/23%) of the maximum recommended daily sodium intake. Six products (8.3%) contained more than 500 mg sodium/tablet. Vitamin products contained significantly more sodium than magnesium (p=0.004), calcium (p=0.006) and mineral (p=0.048) products; this might be due to different solubility properties. The sodium content of the maximum daily dose of pain/common cold drugs was significantly higher than the sodium content of the maximum daily dose of calcium/vitamin D drugs (p<0.0001) and cough drugs (p=0.007). Yet, the majority of the general population and healthcare professionals alike are unaware of the high sodium content of effervescent tablets.[11]

A relevant proportion of the population regularly consumes effervescent tablets as a dietary supplement and/or drugs.[12] In a cross-sectional study from France including 1043 healthy individuals, 26.9% of the participants reported regular intake of effervescent tablets (once in the last 30 days) and 7.3% reported intake of two or more effervescent tablets/week during the last 30 days.[12] A vast majority of 93.8% of these effervescent tablets were OTC drugs and nutritional supplements, such as vitamins.[12] The presence of hypertension, which should require table salt/sodium restriction, did not result in a reduced intake of effervescent tablets.[12]

According to the Federal Statistical Office of Germany (Statistisches Bundesamt, Destatis), the production of dietary supplements in 2020, which include effervescent

Table 3 Sodium content of OTC effervescent tablets

Category	Brand name (manufacturer)	Sodium content/ tablet (mg)	% of the maximum recommended daily sodium intake* of one tablet	Sodium content of maximum recommended daily dose (mg)	% of maximum recommended daily sodium intake* of the maximum recommended daily dose	Maximum recommended tablets per day	OTC	Active ingredients	Sales figures
Pain/common cold (frequently dispensed products)	Aspirin Migräne (Bayer)	544	27	3264	163	6	Yes	Aspirin	3.96 million packs of this class sold in 2021 in Germany
	ASS+C-ratiopharm gegen Schmerzen (Ratiopharm)	477	24	2385	119	5	Yes	Aspirin, ascorbic acid	
	ASPIRIN plus C forte (Bayer)	473	24	1419	71	3	Yes	Aspirin, ascorbic acid	
	ASPIRIN plus C (Bayer)	466	23	2796	140	6	Yes	Aspirin, ascorbic acid	
	Togal Kopfschmerz-Brause+Vitamin C (Kyberg Pharma)	459	23	2754	138	6	Yes	Aspirin, ascorbic acid, caffeine	
	Alka-Seltzer classic (Bayer)	445	22	3560	178	8	Yes	Aspirin	
	FIZAMOL 500 mg (Accord Healthcare)	419	21	3352	168	8	Yes	Acetaminophen	
	PARACETAMOL-ratiopharm 500 mg (Ratiopharm)	416	21	3328	166	8	Yes	Acetaminophen	
	WICK DayMed Erkältungsgetränk (WICK Pharma)	157	8	942	47	6	Yes	Acetaminophen, guaifenesin, phenylephrine	
	Grippostad C Stickpack (STADA Consumer Health)	128	6	384	19	3	Yes	Acetaminophen, chlorpheniramine, ascorbic acid, caffeine	

Continued

Table 3 Continued

Category	Brand name (manufacturer)	Sodium content/ tablet (mg)	% of the maximum recommended daily sodium intake* of one tablet	Sodium content of maximum recommended daily dose (mg)	% of maximum recommended daily sodium intake* of the maximum recommended daily dose	Maximum recommended tablets per day	OTC	Active ingredients	Sales figures
Cough (frequently dispensed products)	NAC-ratiopharm 200 mg, (Ratiopharm)	190	10	570	29	3	Yes	Acetylcysteine	5.30 million packs of this class sold in 2021 in Germany
	Fluimucil 200 mg (Zambon)	158	8	474	24	3	No	Acetylcysteine	
	Fluimucil long 600 mg (Zambon)	158	8	158	8	1	No	Acetylcysteine	
	NAC-ratiopharm 600 mg (Ratiopharm)	150	8	150	8	1	Yes	Acetylcysteine	
	ACC akut 600 mg (Hexal)	139	7	139	7	1	Yes	Acetylcysteine	
	NAC 600 akut (1A Pharma)	139	7	139	7	1	Yes	Acetylcysteine	
	Ambrobeta 30 (betapharm Arzneimittel)	127	6	381	19	3	Yes	Ambroxol	
	ACC akut 200 mg (Hexal)	99	5	297	15	3	Yes	Acetylcysteine	
	NAC 200 akut (1A Pharma)	99	5	297	15	3	Yes	Acetylcysteine	
Calcium/ vitamin D3 (colecalciferol; examples of frequently prescribed effervescent tablets)	Calcium Sandoz forte (Hexal)	288	14	864	43	3	Yes	Calcium+vitamin D	52.32 million DDD of the entire class claimed to the expense of the SHI funds in 2021 in Germany[25]
	Calcium D3 acis 1.200/800 (acis Arzneimittel)	105	5	105	5	1	Yes	Calcium+vitamin D	
	CalciCare-D3 forte 1.000 mg/ 880 I.E. (ORION Pharma)	97	5	97	5	1	Yes	Calcium+vitamin D	
	Calcilac 1000 mg/ 880 I.E. (MIBE Arzneimittel)	96	5	96	5	1	Yes	Calcium+vitamin D	
	Osteoplus 1.000 mg/1.000 I.E. (Recordati Pharma)	78	4	78	4	1	Yes	Calcium+vitamin D	
	Calcigen D 600/400 (MEDA Pharma)	52	3	104	5	2	Yes	Calcium+vitamin D	
	Calcium D3-ratiopharm 600/400 (Ratiopharm)	52	3	104	5	2	Yes	Calcium+vitamin D	
	Calcium Sandoz D Osteo 600 mg/400 I.E. (Hexal)	52	3	104	5	2	Yes	Calcium+vitamin D	

Continued

Table 3 Continued

Category	Brand name (manufacturer)	Sodium content/ tablet (mg)	% of the maximum recommended daily sodium intake* of one tablet	Sodium content of maximum recommended daily dose (mg)	% of maximum recommended daily sodium intake* of the maximum recommended daily dose	Maximum recommended tablets per day	OTC	Active ingredients	Sales figures
Other drugs (examples)	Gittalun (Hermes Arzneimittel)	575	29	1150	58	2	Yes	Doxylamine	–
	Zink-ratiopharm 25 mg (Ratiopharm)	325	16	325	16	1	Yes	Zinc	
	Magnesium Verla (Verla-Pharm Arzneimittel)	314	16	942	47	3	Yes	Magnesium	
	Lösferron (MIBE Arzneimittel)	220	11	660	33	3	Yes	Fe-(II)-D-gluconat	
	Magnesiocard 7,5 mmol (Verla-Pharm Arzneimittel)	138	7	276	14	2	Yes	Magnesium	
	Morphin Painbreak akut 20 mg (PB Pharma)	65	3	1170	59	18	No	Morphine	

*Maximum recommended daily sodium intake according to WHO recommendations.[8]
DDD, defined daily doses; OTC, over-the-counter; SHI, statutory health insurance.

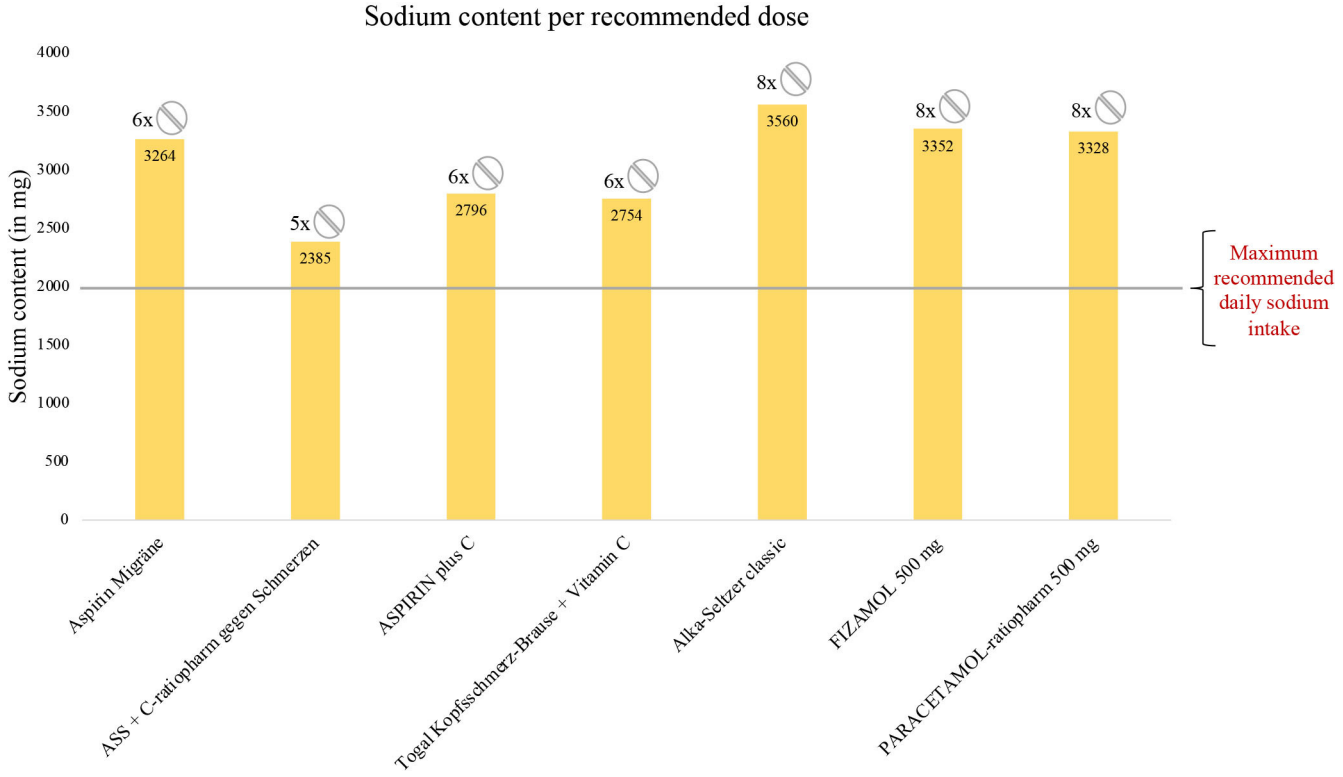

Figure 2 Sodium content of the maximum recommended daily dose of some included effervescent over-the-counter tablets.

tablets, increased by 11% compared with the previous year, most likely as a consequence of the COVID-19 pandemic. In 2020, 180 200 tons of dietary supplements were produced with a value of €1.1 billion in Germany, which corresponds to an increase of 23.4%. In Germany, the sodium content must be indicated on the medicinal products sold in pharmacies but is not mandatory on dietary supplements sold in drugstores or supermarkets.[23 24] Only 5 (13%) of the included dietary supplements available in Germany and only 5.2% of the investigated dietary supplements available in the USA declared sodium content on the packaging, hence, consumers are frequently not informed.

Various sodium-containing drugs administered as effervescent tablets are available. In German pharmacies alone, 3.96 million packages of the included pain/common cold and 5.30 million packs of the included cough effervescent tablets were sold in 2021 (https://www.insight-health.de/ and https://www.datamediq.com/). A total of 52.32 million DDD of calcium/vitamin D drugs, mainly as effervescent tablets, were claimed by community pharmacies at the expense of the SHI funds alone in Germany in 2021.[25] Based on these high sales, we assume that a relevant proportion of the population, occasionally or regularly, consumes effervescent tablets.

A dietary reduction of 1200 mg sodium/day could translate into an annual reduction of 60 000–120 000 new patients with coronary heart disease, 32 000–66 000 fewer strokes and 54 000–99 000 fewer myocardial infarctions in the USA.[13] This amount of sodium is already contained in approximately three of the included effervescent vitamin tablets available in Germany (378.3 mg sodium/tablet on average). A modelling study from China showed that a reduction of 1000 mg table salt/day could prevent approximately 9 million cardiovascular events in China by2030 of which approximately 4 million are fatal.[26] Of note, a total of 1000 mg table salt contains approximately 394 mg sodium. This amount of sodium approximately corresponds to the sodium content of one of the examined vitamin or pain/common cold effervescent tablets.

The intake of one sodium containing dietary supplement effervescent tablet per day for the whole year increases cardiovascular risk more likely than several pain/common cold effervescent tablets/day taken for 5–7 days only. A typical common cold lasts approximately 5–7 days, so the duration of the medical therapy is limited and the intake of OTC-effervescent tablets is rarely permanent. However, studies investigating the (temporary) intake of sodium-containing acetaminophen (paracetamol) effervescent tablets showed an increased risk for hospitalisation for acute heart failure, cardiovascular disease and all-cause mortality.[16 18] The effect of permanent intake of sodium containing dietary supplement effervescent tablet could therefore be higher.

The benefits of pharmacotherapy should always outweigh the risks/side effects. Most likely, the majority of the general population is unaware of the sodium content of effervescent tablets and dietary supplements are often regarded as 'sweets'. Dietary supplements are considered 'foods' by regulators and health benefits of many dietary supplements for healthy, asymptomatic and well-nourished adults have not yet been demonstrated

in randomised clinical trials.[27 28] Consequently, the harm might outweigh the benefit when people ingest several vitamin and electrolyte effervescent tablets daily, assuming they are doing something good for their health. In addition, there is little reason to prescribe effervescent tablets because most active ingredients are also available as tablets not containing sodium.

Limitations

Some limitations of our study should be considered. This study provides relevant insights into the sodium content in dietary supplemental and pharmacy-only effervescent tablets but does not assess the association between the ingestion of these products and cardiovascular outcomes. Therefore, only assumptions can be made. Nevertheless, the included effervescent tablets contained a relevant amount of sodium comparable to prior studies investigating the association between sodium-containing effervescent tablets and cardiovascular risk. We provide sales figures for effervescent tablets sold in pharmacies. The quantity of dietary supplement effervescent tablets from discounters, grocery and drugstores is not publicly available. Measured (Germany) sodium contents of dietary supplements were compared with declared (USA). Assuming the manufacturer declares the correct sodium content on the packing, the detection of national differences is possible. Nevertheless, the assumption that the declared sodium content of dietary supplements available in the USA are valid, is a limitation. It is not guaranteed that the ingredients declared on the packing are 'correct'.[29–31]

CONCLUSION

Dietary supplements and OTC effervescent tablets investigated herein contained high sodium. Some products contain more sodium than others, although comparable in (active) ingredients. As the variability between preparations is high and these amounts of additional sodium intake may contribute to poor BP control and cardiovascular events, including hospitalisation for acute heart failure and death, we think regulators should demand a front-package labelling of sodium content and associated risk before market access. Based on the study findings, patients at risk should be advised to limit effervescent tablets to prevent the ingestion of hidden sodium and to select non-effervescent alternatives containing the same active ingredients. Finally, we suggest that manufacturers should be prompted to reduce sodium in their effervescent formulations.

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REFERENCES

1 Neal B, Wu Y, Feng X, *et al*. Effect of salt substitution on cardiovascular events and death. *N Engl J Med* 2021;385:1067–77.
2 He FJ, Tan M, Ma Y, *et al*. Salt reduction to prevent hypertension and cardiovascular disease: JACC state-of-the-art review. *J Am Coll Cardiol* 2020;75:632–47.

3 Taylor RS, Ashton KE, Moxham T, *et al*. Reduced dietary salt for the prevention of cardiovascular disease: A meta-analysis of randomized controlled trials (Cochrane review). *Am J Hypertens* 2011;24:843–53.
4 He FJ, Li J, Macgregor GA. Effect of longer-term modest salt reduction on blood pressure. *Cochrane Database Syst Rev* 2013;2013:CD004937.
5 He FJ, MacGregor GA. Role of salt intake in prevention of cardiovascular disease: controversies and challenges. *Nat Rev Cardiol* 2018;15:371–7.
6 Huang L, Trieu K, Yoshimura S, *et al*. Effect of dose and duration of reduction in dietary sodium on blood pressure levels: systematic review and meta-analysis of randomised trials. *BMJ* 2020;368:m315.
7 Afshin A, Sur PJ, Fay KA, *et al*. Health effects of dietary risks in 195 countries, 1990–2017: a systematic analysis for the global burden of disease study 2017. *Lancet* 2019;393:1958–72.
8 World Health Organization. *Guideline: Sodium intake for adults and children*. World Health Organization, 2012.
9 Powles J, Fahimi S, Micha R, *et al*. Global, regional and national sodium intakes in 1990 and 2010: a systematic analysis of 24 H urinary sodium excretion and dietary surveys worldwide. *BMJ Open* 2013;3:e003733.
10 He FJ, Burnier M, Macgregor GA. Nutrition in cardiovascular disease: salt in hypertension and heart failure. *Eur Heart J* 2011;32:3073–80.
11 Schutte AE, Neal B. The sodium hidden in medication: a tough pill to swallow. *Eur Heart J* 2022;43:1756–8.
12 Perrin G, Berdot S, Thomas F, *et al*. Evaluation of exposure to Effervescent drugs in a large health check-up population in France: a cross-sectional study. *BMJ Open* 2018;8:e022368.
13 Bibbins-Domingo K, Chertow GM, Coxson PG, *et al*. Projected effect of dietary salt reductions on future cardiovascular disease. *N Engl J Med* 2010;362:590–9.
14 He FJ, MacGregor GA. Salt reduction LOWERS cardiovascular risk: meta-analysis of outcome trials. *Lancet* 2011;378:380–2.
15 Brown IJ, Tzoulaki I, Candeias V, *et al*. Salt intakes around the world: implications for public health. *Int J Epidemiol* 2009;38:791–813.
16 Zeng C, Rosenberg L, Li X, *et al*. Sodium-containing acetaminophen and cardiovascular outcomes in individuals with and without hypertension. *Eur Heart J* 2022;43:1743–55.
17 Benitez-Camps M, Morros Padrós R, Pera-Pujadas H, *et al*. Effect of Effervescent paracetamol on blood pressure. *J Hypertens* 2018;36:1656–62.
18 Perrin G, Arnoux A, Berdot S, *et al*. Association between exposure to Effervescent paracetamol and hospitalization for acute heart failure: A Case-Crossover study. *J Clin Pharmacol* 2022;62:883–90. 10.1002/jcph.2027 Available: https://accp1.onlinelibrary.wiley.com/toc/15524604/62/7
19 George J, Majeed W, Mackenzie IS, *et al*. Association between cardiovascular events and sodium-containing Effervescent, Dispersible, and soluble drugs: nested case-control study. *BMJ* 2013;347:f6954.
20 Turtle EJ, Dear JW, Webb DJ. A systematic review of the effect of paracetamol on blood pressure in hypertensive and non-hypertensive subjects. *Br J Clin Pharmacol* 2013;75:1396–405.
21 MacIntyre IM, Turtle EJ, Farrah TE, *et al*. Regular acetaminophen use and blood pressure in people with hypertension: the PATH-BP trial. *Circulation* 2022;145:416–23.
22 Ubeda A, Llopico J, Sanchez MT. Blood pressure reduction in hypertensive patients after withdrawal of Effervescent medication. *Pharmacoepidemiol Drug Saf* 2009;18:417–9.
23 Bundesministerium der Justiz, Bundesamt für Justiz. Verordnung Über Nahrungsergänzungsmittel (Nahrungsergänzungsmittelverordnung - Nemv). 2017:2011–3.
24 Europäisches Parlament. *RICHTLINIE 2002/46/EG DES EUROPäISCHEN PARLAMENTS UND DES RATES Vom 10. Juni 2002 Zur Angleichung der Rechtsvorschriften der Mitgliedstaaten Über Nahrungsergänzungsmittel*. 2017;21:1–37.
25 Ludwig W-D, Mühlbauer B, Seifert R, *et al*. Arzneiverordnungs-report 2021. Springer; 2021.
26 Tan M, He F, Morris JK, *et al*. Reducing daily salt intake in China by 1 G could prevent almost 9 million cardiovascular events by 2030: a Modelling study. *BMJNPH* 2022;5:164–70.
27 Ronis MJJ, Pedersen KB, Watt J. Adverse effects of Nutraceuticals and dietary supplements. *Annu Rev Pharmacol Toxicol* 2018;58:583–601.
28 Moyer MW. Nutrition: vitamins on trial. *Nature* 2014;510:462–4.
29 Andrews KW, Gusev PA, McNeal M, *et al*. Dietary supplement ingredient database (DSID) and the application of analytically based estimates of ingredient amount to intake calculations. *J Nutr* 2018;148:1413S–21S.
30 Cohen PA, Avula B, Wang Y-H, *et al*. Quantity of melatonin and CBD in melatonin Gummies sold in the US. *JAMA* 2023;329:1401–2.
31 Tucker J, Fischer T, Upjohn L, *et al*. Unapproved pharmaceutical ingredients included in dietary supplements associated with US food and Drug Administration warnings. *JAMA Netw Open* 2018;1:e183337.