

INVITED PAPER

When good intentions go wrong: Paracetamol formulations contain hidden sodium

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There are likely millions of people worldwide taking paracetamol on a daily basis. Paracetamol is one of the most commonly used over-the-counter painkillers used to treat aches, pains, or as part of cold and flu remedies. In the United Kingdom alone, there were in 2014 some 42 million paracetamol-containing medicines prescribed with a further 200 million packs sold over the counter.¹ This equates to about 6,300 tons of paracetamol sold each year in the UK with the figure for France close to 10,000 tons. Some paracetamol formulations contain large quantities of sodium, namely those that are typically indicated as 'fast-acting' or 'fizzy' and by taking these medications regularly, people are unknowingly increasing their risk for raised blood pressure and cardiovascular disease.²

In a recent paper by Zeng and colleagues in the *European Heart Journal*,³ the authors compared the risks of incident cardiovascular disease and all-cause deaths among people who started to take sodium-containing paracetamol to those who started to take paracetamol, but without sodium. They used an electronic medical record database of approximately 17 million patients in the United Kingdom, and focused on people with hypertension and those without. In people with hypertension (N=151,398) and without (N=147,299) they consistently found that the use of sodium-containing paracetamol was associated with increased risks of cardiovascular disease and all-cause deaths, with the hazard ratio being 1.59 (95%CI 1.32-1.92) in those with hypertension and 1.45 (1.18-1.79) in those without hypertension. Risks across different cardiovascular outcomes, including myocardial infarction and stroke, were found in both those with and without hypertension.

It is important to realise that these paracetamol formulations contained a high amount of sodium, approximately 390 to 440 mg of sodium per tablet. If a person takes a full dose of paracetamol regimen, this would lead to over 3000 mg of additional sodium consumed per day – far exceeding the WHO daily limit of 2000 mg.⁴

For some time now, a reduction in salt intake has been considered a 'best buy'. Multiple national and international blood pressure guidelines, as well as the World Health Organisation, recommend that daily sodium intake should not exceed 2000 mg (~1 teaspoon of salt).⁴ In turn, many government and non-governmental organisations advocate strongly for actions to reduce population sodium intake, with some interventions targeting public education, and industry reformulation of packaged foods among others. Most recently a global call to action was again published by the World Hypertension League and the International Society of Hypertension.⁵ This is with good reason. The Global Burden of Disease study showed excess sodium intake to be among the leading dietary risks estimated to cause 3 million deaths around the world every year.⁶ And a large, cluster-randomised trial recently showed that by lowering sodium intake (using a potassium-containing salt substitute with 25% less sodium chloride) not only lower blood pressure but also lower rates of stroke, major cardiovascular events and all-cause deaths.⁷

It therefore seems rather counterintuitive that millions of people are consuming large amounts of sodium unknowingly, while the World Health Organisation and many other organisations are

strongly calling for actions and awareness to lower sodium or salt intake. Note, that it is not only paracetamol formulations that contain sodium. This is also relevant to many other effervescent, dispersible and soluble fast-acting medications and vitamin pills that contain large quantities of hidden sodium, mostly being available over the counter (Table). For example, a single 5g sachet of effervescent antacids contain about 850 mg of sodium, and fizzy vitamins approximately 280 mg of sodium. In a study done in France, more than 1 in 4 of the general population who underwent medical check-ups had consumed 'fizzy' tablets in the past 30 days.⁸ Nine in 10 of these were instances of self-medication, with paracetamol, aspirin, vitamins and betaine accounting for 95% of tablets used.⁸

What is also striking is that the paper by Zeng et al.³ is not the first to demonstrate this. Their findings are highly aligned with previous similar papers, most notably a report done in 2013 by George and colleagues.⁹ In following 1.3 million patients over 7.2 years that included 61,000 patients with an incident cardiovascular event and matched controls, they reported odds ratios for cardiovascular events consistent with those reported by Zeng and colleagues. There was also in the report an odds ratio of 7.18 (6.74 to 7.65) for hypertension in individuals exposed to sodium-containing drugs.⁹

With global calls for action to reduce salt intake, similarly these findings should not remain hidden. In an accompanying editorial,² we highlight that there is an immediate need to protect consumers against the risk of hidden sodium in over-the-counter medications. Perhaps the best approach

is to require the mandatory labelling of all medications containing significant quantities of sodium with a front-of-pack warning label. Similar to general calls for action to reduce salt intake,⁵ programs are required that raise public and practitioner awareness of the hidden sodium in medications, to educate about the need to avoid effervescent, dispersible, and soluble medicines in all but essential circumstances.

References

1. Moore RA, Moore N. Paracetamol and pain: the kiloton problem. *Eur J Hosp Pharm.* 2016;23:187-188. doi: 10.1136/ejhpharm-2016-000952
2. Schutte AE, Neal B. The sodium hidden in medication: a tough pill to swallow. *Eur Heart J.* 2022;10.1093/eurheartj/ehab888. doi: 10.1093/eurheartj/ehab888
3. Zeng C, Rosenberg L, Li X, Djousse L, Wei J, Lei G, Zhang Y. Sodium-containing acetaminophen and cardiovascular outcomes in individuals with and without hypertension. *Eur Heart J.* 2022; <https://doi.org/10.1093/eurheartj/ehac059>.
4. World Health Organization. SHAKE the Salt Habit. The SHAKE Technical Package for Salt Reduction. In: Geneva, Switzerland: WHO; 2016.
5. Campbell NRC, Whelton PK, Orias M, Wainford RD, Cappuccio FP, Ide N, Neal B, Cohn J, Cobb LK, Webster J, et al. 2022 World Hypertension League, Resolve To Save Lives and International Society of Hypertension dietary sodium (salt) global call to action. *J Hum Hypertens.* 2022:1-10. doi: 10.1038/s41371-022-00690-0

Table. Sodium content of several over-the-counter medicines¹⁰

Medication		Amount of sodium (mg)
Antacids	(e.g. Alka-Seltzer), single sachet of powder or a tablet (weighing 5g)	850
Heartburn relief	(e.g. Eno, per 5g dose)	843
Soluble pain killers	(per tablet)	up to 500
	(Panadol soluble 500mg tablet)	425
Urinary alkalinisers	(sachet of Ural (4g)	644
	(sachet of Citravesent)	396
Fizzy vitamins	(Berocca effervescent tablet)	271-287
	(Redoxon effervescent tablet)	312

6. GBD 2017 Diet Collaborators. Health effects of dietary risks in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2019;393:1958-1972. doi: 10.1016/s0140-6736(19)30041-8

7. Neal B, Wu Y, Feng X, Zhang R, Zhang Y, Shi J, Zhang J, Tian M, Huang L, Li Z, et al. Effect of Salt Substitution on Cardiovascular Events and Death. *N Engl J Med*. 2021;385:1067-1077. doi: 10.1056/NEJMoa2105675

8. Perrin G, Berdot S, Thomas F, Pannier B, Danchin N, Durieux P, Sabatier B. Evaluation of exposure to effervescent drugs in a large health

check-up population in France: a cross-sectional study. *BMJ Open*. 2018;8:e022368. doi: 10.1136/bmjopen-2018-022368

9. George J, Majeed W, Mackenzie IS, Macdonald TM, Wei L. Association between cardiovascular events and sodium-containing effervescent, dispersible, and soluble drugs: nested case-control study. *Bmj*. 2013;347:f6954. doi: 10.1136/bmj.f6954

10. Saxelby C. The hidden sources of sodium in medicines and additives. <https://foodwatch.com.au/blog/additives-and-labels/item/the-hidden-sources-of-sodium-in-medicines-and-additives.html>. Accessed 23 November.

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