

## **Climate change and melting medications**

Bernadette Macrohon<sup>1</sup>, Medine I. Gulcebi<sup>2</sup>, Sanjay M. Sisodiya<sup>3</sup>

1. Zamboanga City Medical Center and Ateneo de Zamboanga University School of Medicine, Philippines

2. Department of Medical Pharmacology, Marmara University School of Medicine, Istanbul, Turkey.

3. Sanjay M. Sisodiya, Department of Clinical and Experimental Epilepsy, UCL Queen Square Institute of Neurology, Queen Square, WC1N 3BG, UK

Author for correspondence: Sanjay Sisodiya, [s.sisodiya@ucl.ac.uk](mailto:s.sisodiya@ucl.ac.uk)

The mother of a 10-year old child with epilepsy asked if the child's treatment could be switched from valproate syrup to tablets for family finance reasons, as she could not afford to pay for an entire bottle of syrup in one go, but could buy a few tablets at a time. To introduce tablets to the child, the pediatric neurologist gave his mother free samples from a pharmaceutical representative, transported in his car and subsequently stored in the clinic (air-conditioned for appointments) prior to dispensation. Opening one blister to show her son a tablet, the mother found it melted (Figure: A, compared to intact tablet, B, from a separate batch) and unusable.

Patients attending sparse pediatric neurological services in the Philippines may travel for hours using non-air-conditioned transport. Each valproate tablet costs them 42 pesos: the average Philippine daily wage is 386 pesos. Patients may not have facilities to keep medications within stipulated storage parameters. On this occasion, medication storage partly occurred in the representative's car during a period of extreme unseasonal heat, with a peak heat index (a measure of what the temperature 'feels like', incorporating temperature and humidity<sup>1</sup>) of 42°C, classed locally as 'danger level'<sup>1</sup>.

Exposure to extreme temperatures and/or humidity may impact the physicochemical stability of medications, potentially leading to therapeutic failure or adverse drug reactions<sup>2</sup>. Drug formulations that are not optimized for stability in developing countries with tropical climates may demonstrate compromised biopharmaceutical characteristics<sup>3</sup>. Prolonged exposure to high temperatures and/or humidity may lead to interactions among formulation components that reduce in vitro dissolution of oral solid dosage forms, in other words the release of the drug from its formulation, and consequently, may alter oral bioavailability. All these factors could lead to significant variability in drug absorption, potentially impacting clinical efficacy, which is particularly important for drugs with a narrow therapeutic window or when switching brands, where altered drug bioavailability may result in adverse outcomes due to reduced physicochemical stability.

Valproate tablets should be stored below 25°C. It is reportedly stable under extreme temperatures, but being hygroscopic, may be unstable in humid environments<sup>4</sup>.

Climate change may have a variety of effects on medications commonly used for people with epilepsy<sup>5</sup>, including the disruption of supply chains, though there are no previous reports of tablets melting in high temperatures and humidity, to our knowledge. As climate change makes heatwaves and days of extreme temperatures and humidity more frequent, medication supply chains will have to adapt. As is often the case, climate change will act as a multiplier for factors causing global health inequalities, amongst which is the lack of provision of medicines to tackle the treatment gap in epilepsy.

### **Conflict of interest**

BM and MGI declare no conflict of interest. SMS has received honoraria for educational events or advisory boards from Jazz Pharma, Angelini Pharma, Biocodex, Eisai, Zogenix/UCB

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### **Ethical publication statement**

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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**Figure Legend. Melted medication.** Two medication blisters are shown, both for valproate tablets, one melted (A), the other intact for comparison (B).