TEMPERATURE
2016, VOL. 3, NO. 1, 43–45
http://dx.doi.org/10.1080/23328940.2016.1139963

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FRONT MATTER: LETTER

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Seeking the tropical heat – a matter of microbes?

Letter on: Romanovsky AA. Protecting western redcedar from deer browsing—with a passing reference to TRP channels. Temperature 2015; 2:142–9; http://dx.doi.org/10.1080/23328940.2015.1047078

Dear Editor-in-Chief,

This letter is in response to the puzzle posed in the recent editorial published in Temperature.[1] Some of the most intriguing aspects of thermobiology involve thermomimetic botanical compounds that produce sensations of heat and cold. The best studied of these is capsaicin, the main pungent ingredient in chili peppers. Capsaicin exerts many of its biological effects in humans and other mammals by binding to and activating TRPV1, a nonselective cation channel expressed in a subset of sensory neurons responsible for triggering the sensation of pain.[2] This same channel can be activated by noxious heat (>42°C), accounting for the similar perceptions evoked by piquant spice and high temperatures and the use of the English word "hot" to describe both. Other stimuli, including protons and certain endocannabinoid lipids, can also activate TRPV1. In fact, whereas heat and protons activate TRPV1 orthologs in a wide range of vertebrate species, sensitivity to capsaicin and related vanilloid compounds appears to be restricted to mammalian TRPV1.

Despite the aversive sensory experience associated with capsaicin exposure, a substantial fraction of the world's population consumes foods rich in this compound on a daily basis. Through cultural indoctrination, children and adolescents in many nations "acquire a taste" for spicy foods through repetitive exposure. It has long been recognized that people living in hotter climates tend to consume spicier foods, including those containing more capsaicin, than individuals in cooler climates. Yet, as pointed out in reference,[1] the basis of this interesting biocultural trend remains unresolved.

Why might capsaicin consumption be greater in hotter climates? There are reports that capsaicin exhibits potentially beneficial neuroprotective, anti-inflammatory, and anti-epileptic activities. However, there is no apparent reason why dietary practices related to these or analogous health effects would be related to local climate. The same argument can be made for the possibility that social advantages emanate from demonstrating a tolerance to spicy foods. Although social gain might encourage individuals to overcome their natural aversion to capsaicin's pungency, it is not evident that this would be a climate-dependent phenomenon.

Perhaps the most widely cited rationale for the spicy food-climate connection has been that the thermoregulatory effects of capsaicin consumption enhance comfort in hot climates. Acute administration of capsaicin and related TRPV1 agonists produce hypothermia in most mammalian species.[3] This effect is mediated by a combination of decreased heat production, cutaneous vasodilation, and cold-seeking behavior. In humans, these effects also include gustatory sweating. In rodents, the hypothermic effects of capsaicin are completely dependent on TRPV1. Conversely, pharmacological antagonism of TRPV1 produces a transient hyperthermic response. This response has been observed in rodents and humans, is mediated by activation of a pool of TRPV1 somewhere outside the blood-brain barrier, and involves augmentation of sympathetic drive for heat generation, at least in part through brown adipose stimulation. With repetitive exposure to TRPV1 antagonists, the hyperthermic response becomes attenuated.

At face value, these observations appear to be in line with the idea that vanilloid-evoked hypothermia might foster consumption of capsaicin-rich foods in hot climates. However, this interpretation ignores longer-term

effects of repetitive capsaicin administration.[3] Over time, exposure to capsaicin desensitizes TRPV1 and, under some conditions, leads to inactivation and sometimes even degeneration of neurons expressing this channel. As a consequence, rodent body temperature measured days after vanilloid exposure has, in some studies, been found to be elevated. Furthermore, in these studies, rodents desensitized with capsaicin showed impaired abilities to mount an adequate thermoregulatory defense against elevated ambient temperatures. Studies of the long-term effects of capsaicin on human energy metabolism have yielded conflicting results. Yet, on balance they tend to lean toward a small net increase in energy expenditure,[4] contrary to the "capsaicin-as-air-conditioning" hypothesis. Interestingly, food pungency and evoked hypothermia are not inextricably linked. Certain pungent molecules (e.g. agonists of the closely related TRPA1 channel) do not evoke systemic hypothermia, despite the fact that TRPA1 is found in a subpopulation of those sensory neurons that express TRPV1. Taken together, these findings suggest that evoked hypothermia is not the driving force for the association of capsaicin consumption with hot climates.

Perhaps the most compelling potential basis for the preferential consumption of capsaicin-rich foods in hot climates, interestingly enough, has nothing to do directly with either TRPV1 or, for that matter, mammalian thermobiology. Instead, it relates to antibacterial and antifungal properties of capsaicin and certain other spices. Specifically, it has been suggested that, in hot climates, where unrefrigerated foods are more likely to become contaminated with microbes, the robust inclusion of spices serves to suppress the proliferation of these microbes, and thus reduce the likelihood of food poisoning.

A fascinating analysis of this hypothesis was conducted by Billing and Sherman.[5] By examining cookbooks containing traditional recipes from countries around the world, they were able to quantify the number and abundance of spices, including capsaicin, that were called for in recipes for meat dishes. For ten spices, including capsicums, these authors were able to demonstrate a clear correlation between the abundance of spice inclusion in traditional meat recipes and the mean annual temperature of a given country. More importantly, for the purposes of this discussion, they showed that in nations with greater mean temperatures, there was a greater inclusion of those spices that, based on previously published findings, inhibited the growth of a large proportion of tested food spoilage bacterial species. Although capsaicin had been tested on a relatively small number of bacterial species, it inhibited growth in 80% of those tested. In contrast, in the case of spices that inhibit the growth of a smaller fraction of bacterial species, there was no correlation between their use and mean annual temperature. Another finding especially relevant to the issue at hand was that some of the spices exhibiting the greatest temperaturedependent consumption patterns (e.g., coriander, lemongrass, and turmeric) are not especially pungent, nor are they noted for evoking hypothermia. Therefore, these two biological effects associated with capsaicin appear not to have been the drivers for inclusion of these spices in dishes prevalent in hotweather nations. The authors also evaluated spice availability, as an additional potential determinant of culinary use. However, they found that this variable was not likely to drive the climate-dependent differences in the consumption of these spices. In a follow-up study, Sherman and Hash,[6] demonstrated that the use of spices with antimicrobial activity in vegetarian dishes was much more weakly correlated to mean annual temperature. This finding also makes sense, given that vegetable dishes are inherently less susceptible to spoilage than meat dishes.

In light of this "antimicrobial" argument for the climate-related pattern of capsaicin consumption in humans, it is worth considering a related question. Namely, why does the production of capsaicinoid chemicals differ among native *Capsicum* variants? With plants, as with humans, there is a potential temperature connection, since hot, dry climates reportedly provide the most favorable conditions for capsaicin production in domesticated *Capsicum* variants. Yet, a study conducted on native *Capsicum* variants in Bolivia provided evidence that the production of capsaicinoids is correlated with the amount of fungal predation to which these variants are exposed.[7] Moreover, for a given level of exposure to fungal pathogens, plants producing pungent fruit were more resistant to infection than those producing nonpungent fruit. Thus, in both plants and humans, it may be the antimicrobial properties of capsaicin that dictate its environment-dependent utility, and thus drive its production or consumption.

While this explanation provides a plausible basis for the climate-dependent consumption of capsaicin containing foods across cultures, however, it is worth noting that it is not mutually exclusive with other potential biological or

cultural factors, such as those outlined above. Similarly, in plants, the longstanding notion that capsaicinoid production favors seed dispersal by birds, rather than local consumption by mammals, is not invalidated by the concept of microbe-based selection pressure. Rather, in different settings, it is conceivable that multiple biological and cultural forces shape both capsaicinoid production and the incorporation of foods rich in capsaicin into local diets.

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Michael J. Caterina

Department of Neurosurgery, Department of Biological Chemistry
Department of Neuroscience, Neurosurgery Pain Research Institute
Johns Hopkins School of Medicine, 725 North Wolfe St.
Baltimore, MD 21205 USA
caterina@jhmi.edu