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Chemesthesis Pain Reduction from Capsaicin and/or Allyl Isothiocyanate (AITC) When Introducing Humulene and Myrcene

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Abstract

The pain experienced when eating spicy foods such as peppers, wasabi, horseradish, or spicy mustard come from particular natural compounds binding to specific receptors in our mouth on nerve endings communicating with the sensory cortex. When concentrated, compounds humulene and myrcene, both existent in different ratios in varieties of hops (*Humulus lupulus*), bind to the TRPM8 receptor. While bound to this receptor at the same time as either capsaicin is bound to the TRPV1 receptor or allyl isothiocyanate (AITC) is bound to the TRPA1 receptor, the pain from the TRPV1 and TRPA1 is severely reduced or eliminated. Test subjects have volunteered to test the efficacy of the humulene & myrcene concentrate through both formalized controlled environment experiments as well as informal field sample efficacy demonstrations on social media.

Subject Areas

Chemistry, Neurology, Neuroscience, Physiology, Neurochemistry

Keywords

TRPM8, TRPV1, TRPA1, Humulene, Myrcene, Capsaicin, Allyl Isothiocyanate, Sensation, Hops, Spice, Cooling, Burning

1. Introduction

Throughout history, the tingling pain sensation caused by eating spicy foods has both drawn people to and driven people away from, experiencing it. This sensation, Chemesthesis, refers to the sensory perception of chemical compounds, such as capsaicin found in spicy foods, which can induce sensations of heat, burning, tingling, or pain. [1] This sensory experience is distinct from the basic taste sensations (sweet, sour, bitter, salty, umami) and is related to the activation of sensory receptors like the TRPV1 receptor, which is sensitive to capsaicin and responsible for the heat and pain sensations associated with spicy foods. [2]

The sensory cortex, situated in the cerebral cortex of the brain, is a complex neural structure essential for processing and interpreting sensory information from the body's various sensory modalities [3]. This region is parcellated into distinct areas, each specializing in the perception of specific sensory stimuli, including tactile, thermal, auditory, visual, and chemesthetic sensations [1]. The sensory cortex integrates and maps incoming sensory signals, allowing for the conscious perception of stimuli like touch, pain, temperature, sound, and sight. [1] [4] These neural representations of sensory input are further processed, ultimately contributing to the multifaceted and dynamic human sensory experience, enabling recognition, interpretation, and response to the surrounding environment. [4]The relationship between chemesthesis and the sensory cortex is a fundamental aspect of how we perceive and process the sensory experiences associated with chemical compounds, such as those found in spicy foods.

1) **Compounds and Sensory Perception**: Particular compounds can activate specific transient receptor potential (TRP) sensory receptors found in the mucous membranes of the mouth, nose, and other areas of the body. [1]

2) **Sensory Receptors**: Particular sensory receptors, including the TRPV1 (vanilloid type 1), TRPA1 (ankyrin 1), and TRPM8 (melastatin 8) receptors, are sensitive to different chemical compounds and are responsible for detecting sensations like spiciness (TRPV1), irritation (TRPA1), and cooling (TRPM8). [1]

3) **Sensory Cortex Processing**: When consuming spicy foods or making contact with chemesthetic compounds, the activation of these sensory receptors sends signals to the brain. These signals are transmitted to the primary somatosensory cortex, a region in the brain responsible for processing tactile, temperature, and pain sensations. [1] [2] [4]

4) **Brain's Interpretation**: The primary somatosensory cortex processes the incoming sensory information and interprets it, creating the conscious experience of chemesthetic sensations. For example, when capsaicin activates the TRPV1 receptors, the primary somatosensory cortex interprets this signal as a burning or pain sensation. [5] [6]

5) **Integration with Other Sensory Information**: The sensory cortex doesn't work in isolation. It integrates chemesthetic information with other sensory data, such as sight, taste, and smell, to provide a comprehensive perception of the overall sensory experience. This integration can affect how we perceive the flavor and spiciness of foods. [1] [5]

6) **Subjective Experience**: The perception of chemesthetic sensations, like spiciness or cooling, can be highly subjective. Factors such as an individual's genetic predisposition, previous exposure to such sensations, and cultural influences can influence how chemesthetic experiences are perceived and tolerated. [1] [4] [6]

Hops (*Humulus lupulus*) is a flowering plant that has been for the most part relegated to the brewing industry as the bittering offset to the sweetness from the malted grains in beer. This flower holds many different compounds. [7] Two compounds, which bind to the TRPM8 receptor, humulene and myrcene, are terpenes found in hops, and they are known for their roles in contributing to the flavors and aromas of these plants. [7]

Humulene (C15H24), a sesquiterpene, and myrcene (C10H16), a monoterpene, are both lipophilic compounds. [8] This combination leads to the opening of ion channels within the TRPM8 receptor, allowing the influx of cations, particularly calcium (Ca^{2+}) and sodium (Na^{+}). This influx of ions triggers a signaling cascade within the sensory neuron.

The activation of TRPM8 typically leads to a cooling sensation. [9] In the case of humulene and myrcene, they produce a cooling or soothing feeling in the sensory area where the activation occurs. The sensory information generated by the TRPM8 activation would be transmitted to the brain, specifically to the somatosensory cortex, where it is processed and interpreted as a cooling or tingling sensation. [10]

A complex sensory modulation phenomenon, neurological modulation, occurs when the TRPM8 receptor is activated and the TRPV1 and/or TRPA1 receptors are also activated, leading to a reduced perception of pain from TRPV1 and/or TRPA1 activation. [9] Neurological modulation highlights the complexity of the brain's interpretation of sensory input, where the perception of one sensation can modulate or mitigate the perception of another. [5] [9] [10]

2. Method of Testing

First, to demonstrate the efficacy of humulene and myrcene on neurological modulation of chemesthesis, a formula was created by boiling 56.7 g of pelletized hops in 1.42 L of distilled water. The formula was cooled then dispensed in the form of a spray bottle. It was initially tested by the author and his family as a basic test of the theory that hops by themselves played a part in the chemesthesis pain reduction. Each subject in this informal test reported a significant decrease in the painful sensation of consuming approximately 5 ml hot sauce made from ghost peppers (*Capsicum chinense*).

The feedback collected was that the hop spray was effective, eliminating the pain associated with the hot sauce. Additional feedback from the subjects was the highly bitter taste was not enjoyed by the subjects. Another test was conducted with the same batch, but with honey added to sweeten the flavor. Each subject reported greater enjoyment of the flavor with the same results.

In an effort to identify the effects of humulene and myrcene alone, isolates of each were introduced. This subsequent demonstration consisted of 0.00000383 ml of humulene isolate and 0.00000383 ml of myrcene isolate combined with a "tea" made with the 21.1-degree Celsius results following boiling 22.71 L of water with 0.19 kg of hops and 1.42 L of honey (for flavor), cooling it, then pouring the contents into 59 ml spray bottles.

The original subjects reported a significant increase in the effectiveness of this increased humulene and myrcene isolate batch.

To gather more data, a randomized study of 20 adult volunteer subjects agreed to test the efficacy of the spray.

3. Results

Due to the subjective nature of chemesthesis [1], these random subjects were asked to describe their pain tolerance to spicy foods (**Figure 1**) then choose a hot sauce or spicy food, either which included capsaicin or AITC, that they believed created pain beyond their tolerable threshold (**Figure 2**), then afterward spray the elixir in their mouths 5 - 10 times then report on their response (**Figure 3**).

1) 100% neurological modulation occurred at an 85.097% mean reduction in the pain perception. Each subject reported the pain from the hot sauce had dissipated while continuing to have full control of their taste senses.

2) Following the initial spraying, 8 subjects reported the pain returned and they took additional sprays, which eliminated the burning sensation.

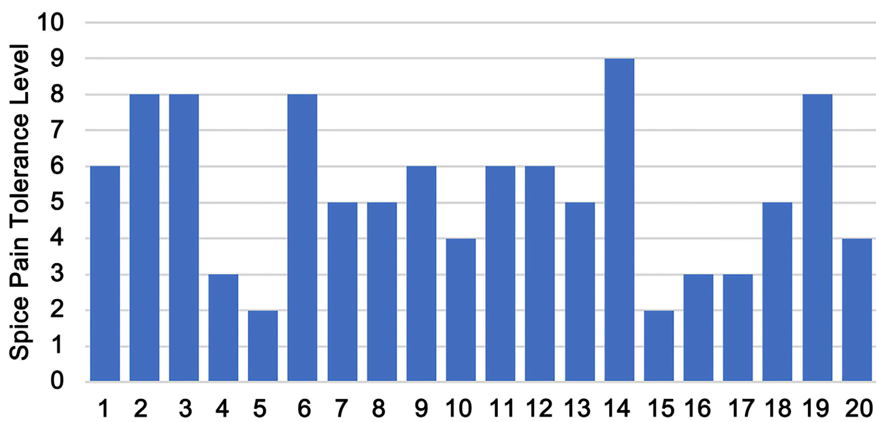

Figure 1. Spice pain tolerance level (1 - 10). 1 = Very low, 10 =Very High.

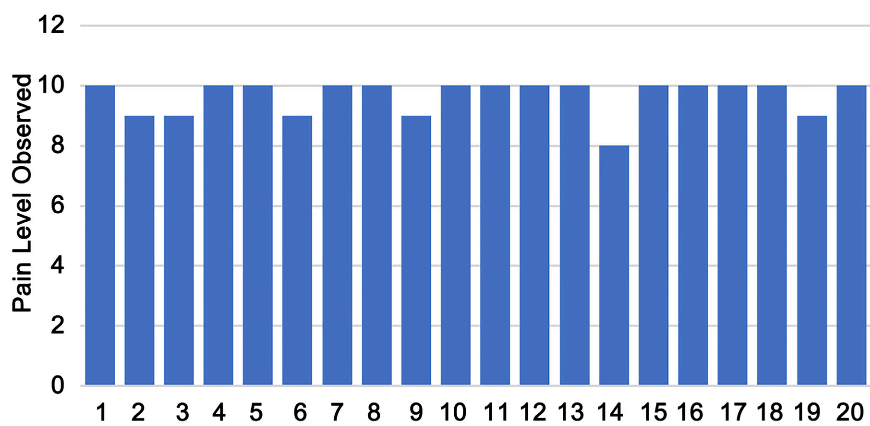

Figure 2. Pain level observed from hot sauce (1 - 10). 1 = Little/No Pain, 10 = Immense Pain.

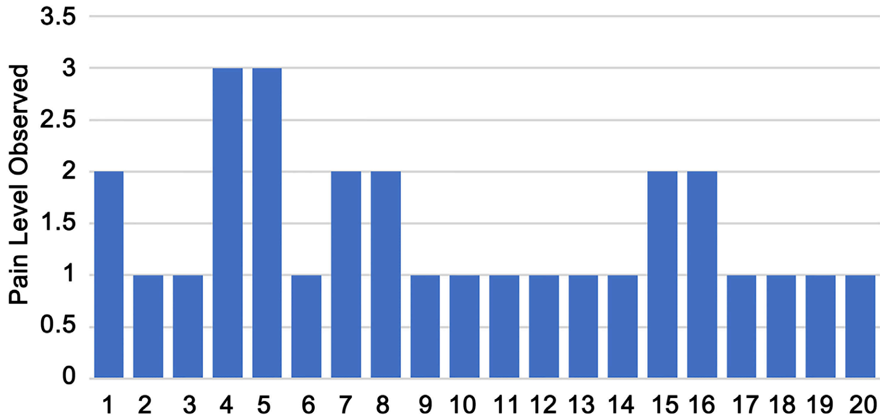

Figure 3. Pain level observed after spray (1 - 10). 1 = Little/No Pain, 10 = Immense Pain.

3) 16 subjects took subsequent tastes of the same hot sauce following the sprays and did not experience the pain they had prior to spraying the elixir in their mouths. 4 did not take additional tastes of the hot sauce.

4) 14 subjects reported that small sips of cold water accentuated the cooling sensation from the spray. 6 subjects did not take sips of water to report.

5) Subjects who consumed the higher Scoville Heat Unit (SHU) foods reported the highest chemesthesis pain experience after eating the hot foods and required, on average, 5 more sprays, to fully eliminate the painful burning sensation.

6) 100% of subjects reported that the next day, they experienced either severely reduced or eliminated "exit burn." This term is associated with the final step of digestion, which, after consuming spicy foods, is usually painful due to the activated TRPV1 and TRPA1 receptors present in our anal glands. Due to the coexistence of the TRPM8 receptor as well, the humulene & myrcene presence in the digestive tract provided neurological modulation in this situation as well.

4. Discussion

The relationship humans have had with spice has been long and complicated, with the compounds of some being used for medicinal purposes, weapons, and flavor enhancement. The recent rise in popularity around the subject includes the television series, "Hot Ones", the Hulu series "Superhot: The Spicy World of Pepper People", and the viral Paqui™ One Chip Challenge. Keeping the topic relevant as a global cultural phenomenon, in 2023, the *Guinness Book of World Records* recognized a new world's hottest pepper. For decades, Pepper Spray has been used as both a self-defense and proactive non-lethal weapon, used across the globe as a personal defense option for individuals as well as by first responders, military, and others.

This research of humulene and myrcene, two compounds that neutralize the pain caused by capsaicin and AITC, introduces options not previously available in the arenas of medicine, military application, culinary circles, and natural remedies. In this study, subjects who could not tolerate the pain of spice found themselves able to consume spicy foods pain-free. This newfound ability opens up a world of cuisine and the benefits that brings. It is the hope of the author to identify new benefits in other areas where the neutralization of pain is possible.

5. Future Research

The Additional areas of study are wide open for the efficacy of the humulene/myrcene benefits in areas of scientific and human benefit. One area would be the neurological modulation benefits in relation to offsetting weaponized irritants such as pepper spray (*oleoresin capsicum*), mustard gas (*bis*(*2-chloroethyl*) *sulfide*), or tear gas, which bind to and activate the TRPV1 and/or TRPA1 receptors in the eyes.

Another area is the relief of chemical and thermal injuries. Both humulene and myrcene may help reduce inflammation associated with chemical and thermal injuries, contributing to pain relief.

Precision of efficacy is another area garnering further research. The author combined isolates with additional ingredients for palatability, which may have created an entourage effect with other hop-based compounds. [11] The addition of honey for improved flavoring was done following initial tests that demonstrated neurological modulation. Increased results have not been attributed to the compounds in honey, albeit subjects reported positive responses to the flavor.

6. Conclusion

This initial randomized study introduces data supporting the evidence that a pain-reducing sensory phenomenon is produced when the activation of the TRPM8 receptor by humulene and myrcene when the TRPV1 and/or TRPA1 are activated. The results of this initial investigation into the effects of humulene and myrcene on the TRPM8 receptor show a highly effective neurological modulation against the activated TRPV1 and TRPA1 receptors.

Conflicts of Interest

The research presented in this paper was conducted by Dr. Curtis Breville as the inventor of Dr. B's Elixir—Cooling Mouth Spray and as a principal with a financial interest in C. H. Breville Enterprises LLC, the entity responsible for producing and marketing the product. The financial interest in C. H. Breville Enterprises LLC is tied to the commercial success of Dr. B's Elixir—Cooling Mouth Spray. While every effort has been made to ensure the integrity and objectivity of this research, readers should be aware of the potential for a conflict of interest that may influence the interpretation and presentation of the findings.

The purpose of this paper was to provide the initial results to the greater research community to test, challenge, and provide the scientific rigor and scrutiny of any germinal product whose immense promise is met with an equally immense dearth of research deserves.

This initial research was carried out in compliance with ethical guidelines and scientific standards. The author is committed to transparency and open discourse regarding this potential conflict of interest and for further information or inquiries, please contact Dr. Curtis Breville, curtis@drbselixir.com.

References

[1] Rhyu, M.-R., Kim, Y., Lyall, V. and Vlachova, V. (2021) Interactions between Chemesthesis and Taste: Role of TRPA1 and TRPV1. *International Journal of Molecular Sciences*, **22**, Article 3360. https://doi.org/10.3390/ijms22073360

[2] Lubova, K.I., Chugunov, A.O., Volynsky, P.E., Trofimov, Y.A., Korolkova, Y.V., Mosharova, I.V., Kozlov, S.A., Andreev, Y.A. and Efremov, R.G. (2020) Probing Temperature and Capsaicin-Induced Activation of TRPV1 Channel via Computationally Guided Point Mutations in Its Pore and TRP Domains. *International Journal of Biological Macromolecules*, **158**, 1175-1183. https://doi.org/10.1016/j.ijbiomac.2020.04.239

[3] Inprasit, C. and Lin, Y.-W. (2020) TRPV1 Responses in the Cerebellum Lobules V, VIa and VII Using Electroacupuncture Treatment for Inflammatory Hyperalgesia in Murine Model. *International Journal of Molecular Sciences*, **21**, Article 3312. https://doi.org/10.3390/ijms21093312

[4] Zhang, Z. and Zagha, E. (2023) Motor Cortex Gates Distractor Stimulus Encoding in Sensory Cortex. *Nature Communications*, **14**, Article 2097. https://doi.org/10.1038/s41467-023-37848-4

[5] Han, P., Su, T., Chen, H. and Hummel, T. (2023) Regional Brain Morphology of the Primary Somatosensory Cortex Correlates with Spicy Food Consumption and Capsaicin Sensitivity. *Nutritional Neuroscience*, **26**, 208-216. https://doi.org/10.1080/1028415X.2022.2031495

[6] Holzer, P. (2011) Transient Receptor Potential (TRP) Channels as Drug Targets for Diseases of the Digestive System. *Pharmacology and Therapeutics*, **131**, 142-170. https://doi.org/10.1016/j.pharmthera.2011.03.006

[7] Móricz, Á.M., Bartoszek, M., Polak, J., Marczewska, P., Knaś, M., Böszörményi, A., Fodor, J., Kowalska, T. and Sajewicz, M. (2023) A Comparison of Quantitative Composition and Bioactivity of Oils Derived from Seven North American Varieties of Hops (*Humulus lupulus* L.) *Separations*, **10**, Article 402. https://doi.org/10.3390/separations10070402

[8] Chen, X., Wang, M.Y., Deng, C.H., Beatson, R.A., Templeton, K.R., Atkinson, R.G. and Nieuwenhuizen, N.J. (2023) The Hops (*Humulus lupulus*) Genome Contains a Mid-Sized Terpene Synthase Family That Shows Wide Functional and Allelic Diversity. *BMC Plant Biology*, **23**, Article 280. https://doi.org/10.1186/s12870-023-04283-y

[9] Stinson, R.J., Morice, A.H. and Sadofsky, L.R. (2023) Modulation of Transient Receptor Potential (TRP) Channels by Plant Derived Substances Used in Over-The-Counter Cough and Cold Remedies. *Respiratory Research*, **24**, Article No. 45. https://doi.org/10.1186/s12931-023-02347-z

[10] Voets, T., Droogmans, G., Wissenbach, U., Janssens, A., Flockerzi, V. and Nilius, B. (2004) The Principle of Temperature-Dependent Gating in Cold- and Heat-Sensitive TRP Channels. *Nature*, **430**, Article 748. https://doi.org/10.1038/nature02732

[11] Christensen, C., Rose, M., Cornett, C. and Allesø, M. (2023) Decoding the Postulated Entourage Effect of Medicinal Cannabis: What It Is and What It Isn't. *Biomedicines*, **11**, Article 2323. https://doi.org/10.3390/biomedicines11082323