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Okayama University research: More than just daily supplements — herbal medicines can treat stomach disorders

(Okayama, 22 January) **In a recent study published in *Scientific Reports*, researchers at Okayama University illustrate the potential of berberine, a herbal Chinese medicine, in reducing inflammation within the digestive tract.**

Inflammatory bowel disease (IBD) is a commonly occurring, painful condition which leads to severe swelling within the stomach and intestine. The goal of IBD treatment is to keep this swelling in check. However, not all patients respond effectively to drugs available for this purpose. Dr.TAKAHARA Masahiro's research team at Okayama University has now shown that berberine, a supplement routinely used for diarrhea and diabetes in China, is also effective in reducing IBD-related swelling.

IBD occurs when specialized cells known as $CD4^+$ T cells found in the digestive system do not function properly. This results in inflammation, or the swelling, bloating and pain associated with IBD. Berberine is extracted from shrubs such as tree turmeric and is known to have anti-inflammatory properties. Furthermore, it activates AMPK, a protein responsible for controlling the growth and survival of all eukaryotic cells including $CD4^+$ T cells. Based on these characteristics of berberine the team sought out to examine whether the supplement might be helpful in IBD.

$CD4^+$ T cells were isolated from lamia propria of colitic mice with severe intestinal inflammation and were subsequently treated with berberine. For inflammation to ensue $CD4^+$ T cells first have to release chemicals known as cytokines. The cytokine levels in the isolated $CD4^+$ T cells were therefore substantially high. However, these cytokine levels dropped soon after berberine treatment. To investigate what specifically drove the cytokine plummet, the researchers artificially manipulated AMPK within the cells and found that changes in AMPK activity directly altered cytokine levels. This confirmed the notion that berberine reduced the inflammation caused by $CD4^+$ T-cells by virtue of its AMPK-modulating activity. These effects of berberine were then tested in same colitic mice as above. As observed in the cells, not only was cytokine release greatly reduced in the gut of these mice, but AMPK activity was also high.

The gut harbors various species of bacteria within it, the composition of which directly impacts gastrointestinal health. Therefore, the gut microbes of these mice were also carefully examined. Berberine treatment seemed to reduce the species of certain bacteria, making the composition more homogenous. However, whether this modification of bacterial makeup plays a role in the protective mechanism of berberine is yet to be determined.

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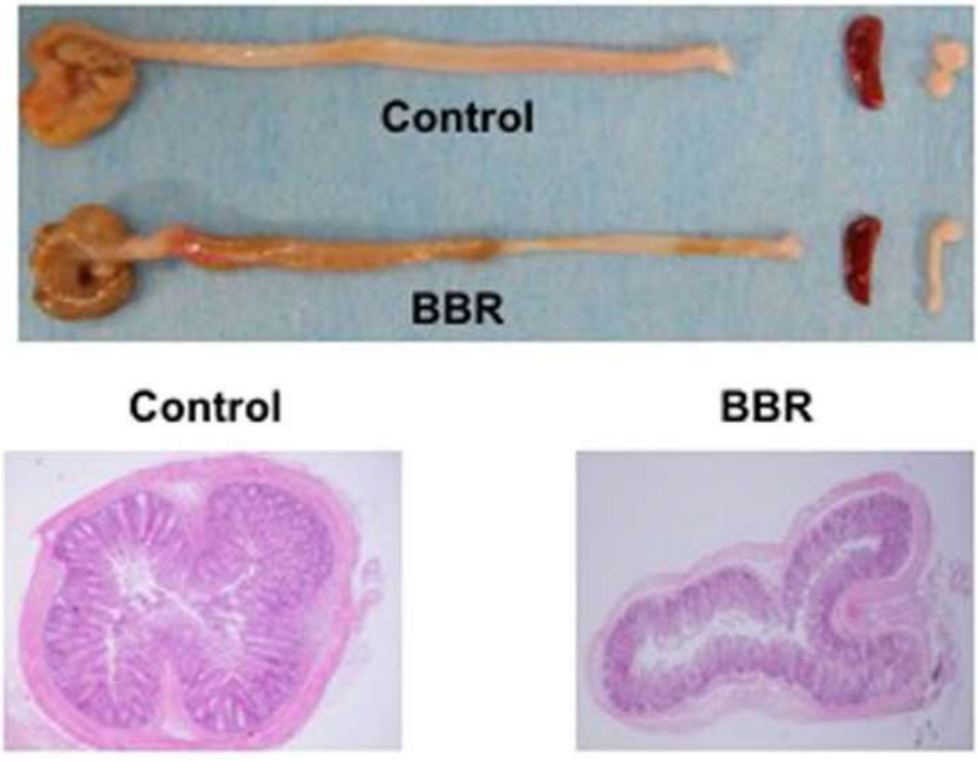
"In summary, we showed for the first time that [berberine] ameliorated $CD4^+$ T cell-related chronic colitis in a mouse model with changes in gut microbiota via AMPK activity", concludes the research team. Targeting AMPK in these cells opens a new avenue for IBD treatment which needs to be explored further.

Background

T cells and inflammation: T cells are protective cells that prevent infections by warding off microbes. A subgroup of T cells, known as helper T cells detect potentially dangerous stimuli and release chemicals known as cytokines. $CD4^+$ T cells are an example of such T cells. The release of cytokines sets in motion a chain of events leading to swelling, redness, heat, and pain (collectively called inflammation) thereby creating a detrimental environment for microbes. The helper T cells of certain individuals do not function properly and release cytokines even in a situation that does not normally react excessively. This leads to disorders such as IBD, wherein certain internal organs are always inflamed.

AMPK: AMPK or 5' adenosine monophosphate-activated protein kinase is a protein that regulates energy production within the cell. AMPK indirectly controls the cellular fate by driving growth, cell division, metabolism and response to stress. By virtue of its role, AMPK is now a popular therapeutic target and drugs that modulate AMPK activity are being investigated for chronic inflammation, obesity, diabetes and hyperlipidemia.



Caption

Sections of the intestine appear healthier and less inflamed in berberine (BBR)-treated mice compared to the controls.

Reference

Masahiro Takahara, Akinobu Takaki, Sakiko Hiraoka, Takuya Adachi, Yasuyuki Shimomura, Hiroshi Matsushita, Tien Thi Thuy Nguyen, Kazuko Koike, Airi Ikeda, Shiho Takashima, Yasushi Yamasaki, Toshihiro Inokuchi, Hideaki Kinugasa, Yusaku Sugihara, Keita Harada, Shingo Eikawa, Hidetoshi Morita, Heiichiro Udono & Hiroyuki Okada. Berberine improved experimental chronic colitis by regulating interferon-γ- and IL-17A-producing lamina propria $CD4^+$ T cells through AMPK activation. *Scientific Reports*, (2019) 9:11934.
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Okayama University is one of the largest comprehensive universities in Japan with roots going back to the Medical Training Place sponsored by the Lord of Okayama and established in 1870. Now with 1,300 faculty and 13,000 students, the University offers courses in specialties ranging from medicine and pharmacy to humanities and physical sciences.

Okayama University is located in the heart of Japan approximately 3 hours west of Tokyo by Shinkansen.

Website: http://www.okayama-u.ac.jp/index_e.html

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