

The anti-inflammatory activity of honey

Introduction

Inflammation is an essential part of the body's response to infection or damage of tissues. It is what starts off the immune response to infection, what starts off the removal of damaged tissue to get a clear site for repair to occur, and what starts off the repair processes to replace damaged tissues. But when there is **excessive** inflammation the consequences of this can range from discomfort to extreme pain, damage to tissues which can be very serious, and scarring which can be very disfiguring.

Pharmaceutical anti-inflammatory drugs are very widely used, but their use is limited by their having harmful side-effects. For example, although inflammation in the wound is the reason wounds remain non-healing, anti-inflammatory drugs are not used on wounds because they slow the healing processes. Similarly they cannot be used in the eyes. Honey has a potent anti-inflammatory activity and does not slow the healing of wounds^{1,2}, and has been safely used to treat infection and damage in the eyes³⁻⁹.

The Ancient Greek physician and herbalist Dioscorides recognised the anti-inflammatory properties of honey, writing that honey is "good for sunburn and spots on the face" and that "honey heals inflammation of the throat and tonsils"¹⁰. This bioactivity of honey is far less well known than its antibacterial activity, but there is a very large amount of evidence for it in publications in modern medical and scientific journals. This article outlines this evidence. (A list of the published papers given as references is at the end of the article.)

In these outlines it is seen that the anti-inflammatory activity of honey minimises scarring,. Also, when honey is used on burns it prevents inflammation from progressing and leading to more damage beyond that caused by the heat.

Summary of evidence

Clinical trials	Reference
A trial was conducted with 16 patients given radiotherapy for head and neck cancer. This normally causes inflammation in the lining of the mouth that is so painful that treatment has to be suspended, the mouth becoming too painful to allow eating. The patients were given honey to hold in the mouth before each radiation treatment began. Fifteen of the patients were able to complete their treatment without suspension, the pain being mild enough to allow eating.	11
Forty patients with head and neck cancer requiring radiotherapy were divided into two groups to receive either radiation alone or radiation plus 20 ml of pure honey 15 min before and 15 minutes and 6 hours after radiation therapy. Patients were evaluated every week for the development of inflammatory damage to the inside of the mouth which is a consequence of the radiation. There was very highly significant reduction in symptomatic-grade inflammation with the honey-treated patients compared with those not given honey; i.e. it was seen in only 20% of the patients given honey compared with 75% not given honey.	12
A trial was conducted on 45 patients using honey to treat various ophthalmological inflammatory conditions. There was improvement in more than 85% of the 48 cases of keratitis (inflammation of the cornea) and 30 cases of conjunctivitis (these not being due to bacterial infection), and 80% of the 15 cases of blepharitis (inflammation of the eyelids).	4

<p>Forty patients diagnosed with head and neck cancer were entered into the trial. Enrolled patients were randomised to either the treatment group, receiving chemotherapy and radiotherapy plus prior topical application of pure natural honey, or the control group, receiving chemotherapy and radiotherapy without honey.</p> <p>In the honey-treated group, patients were advised to smear the inside their mouth with 20 ml of pure honey, 15 minutes before, 15 minutes after and 6 hours after radiation therapy throughout the course of radiotherapy. They were advised to rinse honey on the oral mucosa and then to swallow it slowly, in order to smear it onto the mucosa.</p> <p>Patients were evaluated clinically every week to assess development of mucositis. The honey treatment gave significantly less mucositis: with honey, no patients developed grade four (most severe) mucositis and only three patients (15 per cent) developed grade three mucositis. In the control group, 13 patients (65 per cent) developed grade three or four mucositis.</p>	13
<p>Forty patients diagnosed with head and neck cancer were entered into the trial. Enrolled patients were randomised to either the treatment group, receiving radiotherapy plus prior topical application of pure natural honey, or the control group, receiving radiotherapy with rinses of saline instead of using honey.</p> <p>In the honey-treated group, patients were advised to smear the inside their mouth with 20 ml of pure honey, 15 minutes before, 15 minutes after and 6 hours after radiation therapy throughout the course of radiotherapy. They were advised to rinse honey on the oral mucosa and then to swallow it slowly, in order to coat the mucosa.</p> <p>Patients were evaluated clinically every week to assess development of mucositis. The honey treatment gave very highly significantly less mucositis, the average score for severity with the honey treatment being less than 25% of that with saline rinses.</p>	14
<p>A trial was conducted with thirty volunteers randomly allocated to chew or suck either a solidified manuka honey product, or sugarless chewing gum, for 10 minutes, three times a day, after each meal, to measure the effect of honey on gingivitis which is inflammation of the margin of the gums. Bleeding scores for the gums were recorded before and after the 21-day trial period. There was a statistically highly significant reduction in the percentage of bleeding sites (48% reduced to 17% in the manuka honey group, with no significant changes in the control group).</p>	15
<p>A trial was conducted on 45 patients using honey to treat dyspepsia (inflammation of the stomach, which gives chronic or recurrent pain or discomfort). Doses of 30 ml of honey were given before each meal three times a day for 3 months. The patients were followed up for a further 3 months after that. No drugs were used. Two thirds of the patients became symptom-free and had a normal appearance in the stomach on endoscopy and X-ray after a barium meal. A further 16% had their symptoms relieved.</p>	16
<p>A trial was conducted on 40 patients with non-healing leg ulcers to find, amongst other things, the effect on pain of using honey to dress the ulcers. The severity of pain from the ulcers was scored every two weeks for 12 weeks. A decrease in pain was experienced by 50% of the patients. The average pain score over all 40 patients decreased from 1.6 to 1.08, which was a statistically significant decrease.</p>	18

<p>A trial was conducted on 60 children to assess pain after surgical removal of their tonsils. Half of the children were given 5 ml of honey every hour they were awake and the other half were given a similarly coloured serum as a placebo. All were given acetaminophen painkiller as required to relieve pain. The number of doses of painkiller taken was recorded and pain was scored daily. Dosage with honey gave a statistically very highly significant decrease in pain score for two days after surgery and number of painkiller doses required for 7 days.</p>	17
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<p>Trials conducted with animals: burns and wounds</p> <p><i>[Note: In these experiments the wounds were created surgically under sterile conditions so there was no infection present. Thus the decrease in inflammation observed could not have been due to clearance of infection through the antibacterial activity of honey.]</i></p>	
<p>Superficial burns created on the skin of rats were treated with honey or with a sugar solution with a composition similar to honey. Treatment with honey gave a clearly seen decrease in inflammation compared with sugar.</p>	19
<p>Comparisons were made between honey and silver sulfadiazine, and between honey and sugar, on standard deep dermal burns made on Yorkshire pigs. Histology of biopsy samples showed less inflammation in all honey-treated wounds than in those treated with sugar and silver sulfadiazine.</p>	20
<p>Full-thickness wounds were created by cutting away 2x4 cm pieces of skin on the backs of buffalo calves. The wounds were dressed with honey or nitrofurazone, or with sterilised petrolatum. Histology of biopsy samples showed more marked inflammation in the wounds treated with petrolatum and with nitrofurazone than with honey.</p>	21
<p>A 10 mm long incision was made in the skin of rats and the wounds were treated topically or orally with floral honey, honey from bees fed on sugar, or saline. Histology of wound tissue showed that the infiltration of the tissue with chronic inflammatory cells was greatest in the wounds treated with honey from bees fed on sugar, less in those treated topically with floral honey, and least in those treated orally with floral honey.</p>	22
<p>Incisions 3 cm was made on the skin of rabbits and the wounds on half of the rabbits were treated with topical application of honey. The other half remained as untreated controls. Histology of biopsy samples showed that with the honey treatment there were fewer inflammatory cells infiltrating the wound tissue.</p>	23

Other trials conducted with animals	
<p>Mice were injected with various allergens with and without honey added. Allergens cause production of Immunoglobulin E (IgE), the antibody that causes allergic reactions, which give rise to inflammation. The amount of IgE that was produced by the mice was measured using a skin test of the mouse serum on rats. The honey gave almost complete prevention of production of IgE.</p>	24
<p>Inflammation of the colon was induced in rats by administering trinitrobenzene sulfonic acid. The rats were then treated with enemas of honey or an anti-inflammatory steroid, or saline, daily for 3 or 7 days. After the rats had been killed the colon was examined by histology and biochemical markers of inflammation were measured. Honey was found to be as effective as the steroid.</p>	25
<p>Inflammation of the colon was induced in rats by administering 3% acetic acid. Honey or various sugars were administered, orally and as an enema, daily for a period of 3 days before and 1 day after induction.. Induction of colitis was done on the third day using 3% acetic acid. After the rats had been killed the colon was examined by histology and biochemical markers of inflammation were measured. Honey dose-dependently afforded protection against acetic acid-induced colonic damage. There was almost 100% protection with the highest dose (5 g/kg) used, but the sugars had no effect.</p>	26
<p>Ulcerative colitis (inflammation of the colon) was induced in rats by administering trinitrobenzene sulfonic acid. The rats were then treated, in groups of six, with a single enema of manuka honey or sulfasalazine medication (as a positive control) or a combination of manuka honey and sulfasalazine, or not treated (as a negative control). They were killed 2 weeks later to examine the effects of the treatments.</p> <p>Visual examination of the colon showed that manuka honey on its own significantly decreased ulcerative colitis compared with no treatment and treatment with sulfasalazine (to about one sixth of that with the no-treatment control, being twice as effective as sulfasalazine). Histopathology showed that there was severe inflammation (evidenced by infiltration of inflammatory cells) with no treatment, but only mild inflammation with the honey treatment, this being less than with the sulfasalazine treatment. A significant improvement in all of the multiple biochemical markers of inflammation was also seen with the honey treatment.</p>	27
<p>Colitis (inflammation of the colon) was induced in rats by administering trinitrobenzene sulfonic acid, this being a standard model of human inflammatory bowel conditions. The rats were then treated daily for two weeks, in groups of six, with daily oral doses of manuka honey at a dose rate of 5 g/kg body weight in one group and 10 g/kg body weight in another group, or sulfasalazine medication (as a positive control), or not treated (as a negative control). They were killed 2 weeks later to examine the effects of the treatments.</p> <p>Visual examination of the colon showed that manuka honey on its own significantly decreased colitis compared with no treatment and treatment with sulfasalazine (to about one ninth of that with the no-treatment control, being three times more effective than sulfasalazine). Histopathology showed that there was severe inflammation (evidenced by infiltration of inflammatory cells) with no treatment, but only mild inflammation with the honey treatment. A significant improvement in all of the multiple biochemical markers of inflammation was also seen with the honey treatment. There was little difference in effectiveness between the two dose rates of the honey.</p>	28

<p>Rats were pre-treated with honey 30 minutes before alcohol was given to cause inflammatory damage to the stomach. Compared with the rats not given honey, honey provided more than 80% protection from inflammatory damage, which was assessed both visually and by microscopic examination of the stomach tissue.</p>	29
<p>Rats were pre-treated with honey 30 minutes before alcohol was given to cause inflammatory damage to the stomach. The inflammation was measured as the amount of intravenously injected dye released from the circulation into the stomach contents as a result of inflammation causing blood vessels to open up. Honey was found to decrease the amount of dye released compared with no treatment.</p>	30
<p>Rats were pre-treated with honey 30 minutes before the blood supply to the rats' stomachs was shut off for a while then restored, which causes inflammation. (This is the way that stress causes stomach ulcers in people.). The inflammation was measured as the amount of intravenously injected dye released from the circulation into the stomach contents as a result of inflammation causing blood vessels to open up, and by counting the number of sites of damage to the stomach lining. Honey was found to decrease the number of sites of damage and the amount of dye released compared with no treatment.</p>	31
<p>Rats were pre-treated with honey 30–60 minutes before alcohol was given to cause inflammatory damage to the stomach. Damage to the stomach lining was assessed one hour afterwards. The honey gave 78% protection against the inflammatory damage caused by the alcohol.</p>	32
<p>Rats were dosed with honey, given by mouth, mixed with indomethacin, a NOSAID medication, or alcohol, both of which cause inflammation of the stomach. A mixture of sugars as in honey was also used in place of honey. The resulting damage to the lining of the stomach was compared with that in rats dosed with indomethacin or alcohol without honey. At a dose rate of 5 g/kg body weight the honey gave almost complete protection from damage by the indomethacin and 58% protection from the damage by alcohol. The sugar mixture gave no protection.</p>	33
<p>Rats were pre-treated with honey 30 or 90 minutes before alcohol was given to cause inflammatory damage to the stomach. Damage to the stomach lining was assessed one hour afterwards, and was compared with that in rats not given honey. The honey at a dose rate of 1.25 g/kg body weight gave 73% protection against the inflammatory damage caused by the alcohol, and 85% protection at a dose rate of 2.5 g/kg.</p>	34
<p>Rats were pre-treated with honey, once daily for 7 consecutive days, given by mouth, then dosed with indomethacin, a NOSAID medication which causes inflammation of the stomach. The honey gave significantly decreased inflammation of the stomach compared with untreated rats, there being a lower ulcer index, and lower measures of permeability of small blood vessels and the enzyme myeloperoxidase of the stomach (which are features of inflammation).</p>	35

<p>Rats were subjected to surgery on their intestines that was designed to cause adhesions between the intestines, a condition that results from post-operative inflammation. Before closure of the abdominal cavity after the surgery the intestines and peritoneal cavity of some of the rats were then treated with honey, compared with others where this was not done. A very highly significant reduction in adhesions was seen to result from the treatment with honey.</p>	36
<p>Rats were divided into 3 groups of 25 for the study. After surgery to create adhesions by cutting and joining the intestines, in one group the abdominal cavity was filled with intergel (a pharmaceutical product to minimise adhesions), in another group with honey, and in the third (control) group with nothing. After two-week's post-operative period, the rats were reopened surgically to detect adhesions and take sections of intestine for histopathological study. In the group of rats treated with honey the score for adhesions was 73 compared with 120 in the untreated control group, and 80 with the pharmaceutical gel. These differences were statistically highly significant. The anti-inflammatory activity of the honey was confirmed by the histopathology, which showed that in the control group there was massive infiltration of the adhesion tissue by inflammatory cells whereas in the intragel-treated group there was only moderate infiltration, and in the honey-treated group there was only mild infiltration.</p>	37
<p>Bacterial peritonitis was induced in 18 rats by surgically tying off the intestine and puncturing it. The rats were then randomly assigned to three groups, one group having honey put in the peritoneal cavity, one group having glucose syrup put in the peritoneal cavity, and the third group receiving no treatment after the surgery. All animals were killed 14 days later to assess the adhesion score. Levels of tissue antioxidant enzymes were also measured in tissue samples taken from the abdominal wall, to assess how much these had been increased by inflammation, and a biochemical marker of inflammatory damage was also measured.</p> <p>Adhesion scores of the honey treated group were significantly lower (about half) than those for the control group, and about two thirds of those with the glucose treatment (not a statistically significant difference). The levels of antioxidant enzymes and the biochemical marker levels were also significantly higher in the control group and glucose-treated group than the honey-treated group.</p>	38
<p>The paws of rats were inflamed by injection of lipopolysaccharide (a component of the cells walls of bacteria) 1 hour after injection of the paws with 0.5 ml of a 50% solution of honey or solvent extracts of honey. The honey and honey extracts gave a decrease in swelling of the inflamed paws and their sensitivity to pain. Measurement of nitric oxide and prostaglandin E₂, substances produced in inflammation, showed that honey and honey extracts decreased the level of these.</p>	39

<p>Experiments with cultures of leukocytes</p>	
<p>Cultures of monocytes (a type of leukocyte that is involved in inflammation) were activated with substances which cause an inflammatory response. The response was measured as the amount of 'Reactive Oxygen Species' (ROS) produced. Honey, at a concentration of 1%, gave a decrease of up to 60% in production of these. There were large differences between the different types of honey studied in the size of the decrease in production of ROS.</p>	40

<p>Cultures of neutrophils (a type of leukocyte that is involved in inflammation) were activated with a substance which causes an inflammatory response, and the effect of honey on this was studied. The response was measured as the amount of 'Reactive Oxygen Species' produced. Also, the activation of complement in human serum was measured as the amount of damage caused to sheep blood cells, and the effect of honey on this activation was studied. The amount of activation of both inflammatory processes was halved by the presence of less than 1% of some of the types of honey studied, but it needed a 3–5 times higher concentration of the other honeys tested to get this much inhibition of activation.</p>	41
<p>Cultures of macrophages (a type of leukocyte that is involved in inflammation) were activated with substances which cause an inflammatory response. The response was measured as the amount of nitric oxide produced, the production of which is part of the inflammatory response of cells. An ethyl acetate extract of honey, at a concentration equivalent to its content in a 75% solution of honey, gave a decrease of 75% in production of nitric oxide.</p>	42

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