N-Acetil-Glucosamina (NAG)

Glucosamina e NAG inibiscono la produzione di NO indotta da IL-1b nei condrociti, ma NAG inibisce anche la produzione di COX-2 e IL-6

The Journal of Immunology, 2001,166:5155–5160.

N-AcetylglucosaminePreventsIL-1β-Mediated Activation of Human Chondrocytes1

AlexanderR.Shikhman,†KlausKuhn,†NadaAlaaeddine,†andMartinLotz2†*

Abstract

Glucosamine represents one of the most commonly used drugs to treat osteoarthritis. However, mechanisms of its antiarthritic activities are still poorly understood. The present study identifies a novel mechanism of glucosamine-mediatedanti-inflammatory activity. It is shown that both glucosamine and N-acetylglucosamine inhibit IL-1β- and TNF-α-induced NO production in normal human articular chondrocytes. The effect of the sugars on NO production is specific, since several other monosaccharides, including glucose, glucuronic acid, and N-acetylmannosamine, do not express this activity. Furthermore, N-acetylglucosamine poly-mers, including the dimer and the trimer, also do not affect NO production. The observed suppression of IL-1β-induced NO production is associated with inhibition of inducible NO synthase mRNA and protein expression. Inaddition,N-acetylglucosamine also suppresses the production of IL-1β-induced cyclooxygenase-2 and IL-6. The constitutively expressed cyclooxygenase-1, how-ever, was not affected by the sugar. N-acetylglucosamine-mediated inhibition of the IL-1β response of human chondrocytes was not associated with the decreased inhibition of the mitogen-activated protein kinases c-JunN-terminalkinase, extracellular signal-relatedkinase, and p38, nor with activation of the transcription factor NF-kB. Inconclusion, these results demonstrate that N-acetylglucosamine expresses a unique range of activities and identifies a novel mechanism for the inhibition of inflammatory processes.

NAG stimola la proliferazione di tessuto cartilagineo, circondato da condroblasti

Enhanced healing of cartilaginous injuries by N-acetyl-d-glucosamine and glucuronic acid

Yasunori Tamaia, Katsuyuki Miyatakea, Yoshiharu Okamotoa, Yoshimori Takamorib, Koji Sakamotob, Saburo Minamia,

Abstract

We investigated the restorative effect of orally administered glucose, N-acetyl-d-glucosamine (GlcNAc) and glucuronic acid (GlcUA) on the experimentally produced cartilaginous injuries in rabbits. A total of three holes in the left stifle joint, including one in the medial trochlear ridge, and two in the trochlear sulcus (proximal and distal) of articular cartilage were made surgically using a

drill. For the control group, only tap water was administered daily and for the glucose, GlcNAc, GlcUA groups, a water based solution (1 g/head/day) of glucose, GlcNAc, glucuronolactone was administered daily, respectively. We observed the clinical symptoms daily and the condition of the injured part was observed macroscopically and histologically at 3 weeks after the operation. There was no difference in body weight or general conditions among each group. With respect to medial trochlear injury, 1/3 holes were not cured in the control, but all were cured in the glucose, GlcNAc and GlcUA groups, respectively. With respect to the proximal hole, 4/6 in the control group, 3/3 in the glucose and 2/3 in the GlcNAc were not cured. However, 2/3 in the GlcUA were cured. There was significant difference ($p<0.05$) in the proximal holes between the control and the GlcUA. On the total points, there was significant difference ($p<0.05$) between the control and GlcNAc or GlcUA.

On histological examination, the injured parts were covered by fibrous connective tissues in the control and the glucose, whereas in the GlcNAc and GlcUA groups, the massive proliferation of matured cartilaginous tissues was observed, and the regenerated cartilaginous tissues were surrounded by the proliferation of chondroblast cells. In the regenerated tissue, matured cartilage substrate was also observed. Safranin O and Alcian blue stains marked a more significantly dense in the GlcNAc and GlcUA group than in the control ($p<0.01$) in injured parts as well as in non-injured joint cartilage.

Miglioramento dei sintomi da OA dopo somministrazione di latte di soia con NAG (1g/die per 12 settimane)

Jpn Pharmacol.Ther 34;149 JANUARY 2006

Effects and safety of soymilk beverage containing N-acetyl glucosamine on osteoarthritis

K. Hatano Y. Miyakuni K. Hayashida S. Nakagawa –

Abstract

N-acetyl glucosamine is an amino sugar and a monomeric unit of chitin, a polysaccharide forming structural polymers in the exoskeletons of crustaceans. In humans, it exists in skin, cartilage and blood vessel as a component of hyaluronic acid, and bone tissue, cornea and aorta as a component of keratan sulfate. Osteoarthritis is one of the representative diseases, which disturb joint function and decrease the quality of life. One of the possible causes of osteoarthritis is decrease of amount of N-acetyl glucosamine in age, then feeding N-acetyl glucosamine could become its symptom better. In the present study, we assessed the effect and safety of a soymilk beverage containing N-acetyl glucosamine on osteoarthritis of knee joint, in the way of double-blind placebo-controlled, parallel group study. The subjects were 67 adults (male/female: 27/40, age: 54.3 ± 12.8), who felt slight pain, stiffness, and/or discomfort in their knee joints. They had never been treated the knee osteoarthritis by medication. The treatment group was given, once a day for 12 weeks, the test beverage (200mL) containing 1000 mg or more of N-acetyl glucosamine, and the control group was given the soymilk beverage without N-acetyl glucosamine. The results revealed that, the pain on going up and down the stairs and the pain at rest were significantly reduced in the treatment group compared with the placebo group at 8 week. Range of motion (ROM) in the treatment group was also significantly improved compared with the placebo group at 8 week. Blood examination, physical examination and history taking did not reveal any adverse reactions of clinical importance. These results thus demonstrated that the long-term intake of the soymilk beverage containing N-acetyl glucosamine improves the subjective symptom and range of motion in subjects with slight pain, stiffness, and/or discomfort at knee joint.

Glucosamina e insulino-resistenza

Diabetes. 1999 May;48(5):1101-7.

Allosteric regulation of glycogen synthase and hexokinase by glucosamine-6-phosphate during glucosamine-induced insulin resistance in skeletal muscle and heart.

Virkamäki A1, Yki-Järvinen H.

Abstract

Glucosamine infusion induces insulin resistance in vivo, but the effect of glucosamine on intracellular metabolites of the hexosamine pathway, especially glucosamine-6-phosphate (GlcN6P) is unknown. Because of the structural similarity of glucose-6-phosphate (G-6-P) and GlcN6P, we hypothesized that accumulation of this metabolite might alter the activities of enzymes such as glycogen synthase and hexokinase. We infused glucosamine (30 micromol x kg(-1) x min(-1)) to induce insulin resistance in rats during a euglycemic-hyperinsulinemic clamp. Glucosamine induced whole-body insulin resistance, which was apparent after 90 min and continued progressively for 360 min. Despite inducing severe whole-body insulin resistance and decrease in glycogen synthase fractional activity in rectus abdominis muscle (69+/-3 vs. 83+/-1%, P<0.01) and heart (7+/-1 vs. 32+/-4%, P<0.001), glucosamine did not change the glycogen content in rectus and even increased it in the heart (209+/-13 vs. 117+/-9 mmol/kg dry wt, P<0.001). Glucosamine increased tissue concentrations of UDP-GlcNAc 4.4- and 4.6-fold in rectus abdominis and heart, respectively. However, GlcN6P concentrations increased 500- and 700-fold in glucosamine-infused animals in rectus abdominis (590+/-80 vs. 1.2+/-0.1 micromol/kg wet wt, P<0.001) and heart (7,703+/-993 vs. 11.2+/-2.3 micromol/kg wet wt, P<0.001). To assess the possible significance of GlcN6P accumulation, we measured the effect of GlcN6P on glycogen synthase and hexokinase activity in vitro. At the GlcN6P concentrations measured in rectus abdominis and heart in vivo, glycogen synthase was activated by 21 and 542%, while similar concentrations inhibited hexokinase activity by 5 and 46%, respectively. This study demonstrates that infusion of glucosamine during a euglycemic-hyperinsulinemic clamp results in marked accumulation of intracellular GlcN6P. The GlcN6P concentrations in the heart and rectus abdominis muscle reach levels sufficient to cause allosteric activation of glycogen synthase and inhibition of hexokinase.

Endocrinology 140:1151–1157, 1999 DIABETES, VOL. 49, JUNE 2000

High Glucose and Glucosamine Induce Insulin Resistance via Different Mechanisms in 3T3-L1 Adipocytes

Bryce A. Nelson, Katherine A. Robinson, and Maria G. Buse

Abstract

Sustained hyperglycemia induces insulin resistance, but the mechanism is still incompletely understood. Glucosamine (GlcN) has been extensively used to model the role of the hexosamine synthesis pathway (HSP) in glucose-induced insulin resistance. 3T3-L1 adipocytes were preincubated for 18 h in media ± 0.6 nmol/l insulin containing either low glucose (5 mmol/l), low glucose plus GlcN (0.1–2.5 mmol/l), or high glucose (25 mmol/l). Basal and acute insulin-stimulated (100 nmol/l) glucose transport was measured after re-equilibration in serum and insulin-free media. Preincubation with high glucose or GlcN (1–2.5 mmol/l) inhibited basal and acute insulinstimulated glucose transport only if insulin was present during preincubation. However, only preincubation with GlcN plus insulin inhibited insulin-stimulated GLUT4 translocation. GLUT4 and

GLUT1 protein expression were not affected. GlcN (2.5 mmol/l) increased cellular UDP-N-acetylhexosamines (UDP-HexNAc) by 400 and 900% without or with insulin, respectively. High glucose plus insulin increased UDP-HexNAc by 30%. GlcN depleted UDP-hexoses, whereas high glucose plus insulin increased them. Preincubation with 0.5 mmol/l GlcN plus insulin maximally increased UDP-HexNAc without affecting insulin-stimulated or basal glucose transport. GlcN plus insulin (but not high glucose plus insulin) caused marked GlcN dose-dependent accumulation of GlcN-6-phosphate, which correlated with insulin resistance of glucose transport (r = 0.935). GlcN plus insulin (but not high glucose plus insulin) decreased ATP (10–30%) and UTP (>50%). GTP was not measured, but GDP increased. Neither high glucose plus insulin nor GlcN plus insulin prevented acute insulin stimulation (~20-fold) of insulin receptor substrate 1–associated phosphatidylinositol (PI)-3 kinase. We have come to the following conclusions. 1) Chronic exposure to high glucose or GlcN in the presence of low insulin caused insulin resistance of glucose transport by different mechanisms. 2) GlcN inhibited GLUT4 translocation, whereas high glucose impaired GLUT4 “intrinsic activity” or membrane intercalation. 3) Both agents may act distally to PI-3 kinase. 4) GlcN has metabolic effects not shared by high glucose. GlcN may not model HSP appropriately, at least in 3T3-L1 adipocytes.

NAG non induce insulino-resistenza

Metabolism May 1964Volume 13, Issue 5, Pages 466–472

The effect of intravenous N-acetyl-D-glucosamine on the blood and urine sugar concentrations of normal subjects

E.C. Gaulden, M.D. William C. Keating, M.D.

Abstract

Studies of several investigators have suggested that N-Acetylglucosamine may be useful as a sugar substitute feeding in postoperative subjects and patients with diabetes and liver disease. It is incorporated into body tissues, including the liver where it forms glycogen,1 but its removal from the blood is not significantly affected by insulin.3 It is, at the same time, a source of oral and parenteral nitrogen which does not seem to increase blood ammonia as do some of the protein hydrolysates.8 Ten apparently healthy volunteers with normal glucose tolerance test results were chosen as subjects. Following intravenous administration, N-Acetyl-D-Glucosamine metabolism was compared with that of dextrose in a cross-over design by determining glucose and total reducing substances in the blood, and 24 hour excretion of reducing substances in the urine. It was found that intravenous administration of NADG produces little or no significant change in blood dextrose concentration as measured by the orthotoluidine method. The curve of blood dextrose concentrations differed from that obtained when total reducing substancse were determined. The curve of the concentrations of reducing substances in the blood following administration of NADG is parabolic with a gradual return to the baseline. This contrasts with the curve obtained after dextrose administration; the peak is rapidly attained within 1 hour followed by a precipitous drop to baseline or to below control levels. These data strongly suggest that NADG is metabolized into fragments after intravenous administration; however, virtually none is converted to dextrose. Removal of NADG from the blood represents the sum of the fates of this substance within the body. When 100 Gm. are administered intravenously within 1 hour, approximately 30 per cent are excreted in the urine. Some may be excreted in the gut and the remainder are metabolized in the body. Further studies may indicate that NADG is a suitable sugar substitute for diabetics and a useful nutritional supplement for postoperative subjects and patients with liver disease.

ZENZERO

Effetto anti-infiammatorio dello Zenzero su cellule sinoviali isolate di membrana sinoviale o liquido sinoviale stimolato da TNF-alfa: le cellule trattate con Zenzero hanno mostrato un effetto inibitorio comparabile a quello ottenuto con betametasone inibendo la produzione di citochine IL-1 e IL-6

Arthritis. 2012;2012:505842. doi: 10.1155/2012/505842. Epub 2012 Dec 31.

A synoviocyte model for osteoarthritis and rheumatoid arthritis: response to Ibuprofen, betamethasone, and ginger extract-a cross-sectional in vitro study.

Ribel-Madsen S1, Bartels EM, Stockmarr A, Borgwardt A, Cornett C, Danneskiold-Samsøe B, Bliddal H.

Abstract

This study aimed at determining if synovial cell cultures from rheumatoid arthritis (RA), osteoarthritis (OA), and healthy controls (HC) differ and are suitable disease models in pharmacological studies, and tested their response to some anti-inflammatory drugs. Synovial cells were isolated from synovial membrane or joint fluid. Cells were cultivated and exposed to no or TNF-α stimulation without, or in the presence of, betamethasone, ibuprofen, or a standardized ginger extract. Concentrations of a panel of cytokines, growth factors, and chemokines were mapped for each culture and condition. Our cells secreted an increased amount of the cytokines IL-1β, IL-6, and IL-8 in response to TNF-α stimulation in all conditions. OA cells showed a higher IL-6 and IL-8 and a lower IL-1β production, when not stimulated, than RA and HC cells, which were similar. TNF-α stimulation caused similar IL-1β, IL-6, and IL-8 release in all groups. Ibuprofen showed no effect on cytokine production, while ginger extract was similar to betamethasone. Ginger extract was as effective an anti-inflammatory agent as betamethasone in this in vitro model. Cultured fibroblast-like synoviocytes from OA and RA subjects promise to be a useful pharmacological disease model, but further studies, to support results from such a model are needed.

Gingerolo e gingerdione hanno manifestato in modo significativo attività analgesica e antiinfiammatoria inibendo la sintesi di PGE2

Prostaglandins Leukot Med. 1986 Oct;24(2-3):195-8.

Inhibition of human neutrophil 5-lipoxygenase activity by gingerdione, shogaol, capsaicin and related pungent compounds.

Flynn DL, Rafferty MF, Boctor AM.

Abstract

A series of structurally related pungent natural products including capsaicin, gingerol, and gingerdione among others were evaluated and found to be potent inhibitors of 5-HETE biosynthesis in intact human leukocytes, with IC50 values of 100 and 15 microM for capsaicin and gingerdione, respectively. Several compounds within this series were also found to inhibit PGE2 formation, with the most potent being gingerdione (IC50 = 18 microM). These and other data indicate that members of the capsaicin/gingerol family of pungent compounds can act as dual inhibitors of arachidonic acid metabolism, which could account in part for the antiinflammatory and analgesic properties of compounds within this group.

10-gingerolo, l'8-shogaol, e il 10-shogaol inibiscono l'enzima COX 2 riducendo significativamente l'infiammazione.

Fitoterapia. 2011 Jan;82(1):38-43. doi: 10.1016/j.fitote.2010.09.004. Epub 2010 Sep 15.

Cyclooxygenase-2 inhibitors in ginger (Zingiber officinale).

van Breemen RB1, Tao Y, Li W.

Abstract

Ginger roots have been used to treat inflammation and have been reported to inhibit cyclooxygenase (COX). Ultrafiltration liquid chromatography mass spectrometry was used to screen a chloroform partition of a methanol extract of ginger roots for COX-2 ligands, and 10-gingerol, 12-gingerol, 8-shogaol, 10-shogaol, 6-gingerdione, 8-gingerdione, 10-gingerdione, 6-dehydro-10-gingerol, 6-paradol, and 8-paradol bound to the enzyme active site. Purified 10-gingerol, 8-shogaol and 10-shogaol inhibited COX-2 with IC(50) values of 32 μM, 17.5 μM and 7.5 μM, respectively. No inhibition of COX-1 was detected. Therefore, 10-gingerol, 8-shogaol and 10-shogaol inhibit COX-2 but not COX-1, which can explain, in part, the anti-inflammatory properties of ginger.

Attività inibitoria del gingerolo sui canali TRP

Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease - Volume 1772, Issue 8, August 2007, Pages 978–988

TRP channels and pain

Daniel N. Cortright, ,James E. Krause, Daniel C. Broom

Abstract

Since the molecular identification of the capsaicin receptor, now known as TRPV1, transient receptor potential (TRP) channels have occupied an important place in the understanding of sensory nerve function in the context of pain. Several TRP channels exhibit sensitivity to substances previously known to cause pain or pain-like sensations; these include cinnamaldehyde, menthol, gingerol, and icillin. Many TRP channels also exhibit significant sensitivity to increases or decreases in temperature. Some TRP channels are sensitized in vitro by the activation of other receptors such that these channels may be activated by processes, such as inflammation that result in pain. TRP channels are suggested to be involved in processes as diverse as sensory neuron activation events, neurotransmitter release and action in the spinal cord, and release of

inflammatory mediators. These functions strongly suggest that specific and selective inhibition of TRP channel activity will be of use in alleviating pain.

Parità di efficacia con diclofenac nel trattamento dell'OA, ma con un profilo di tollerabilità superiore

J Altern Complement Med. 2012 Jun;18(6):583-8. doi: 10.1089/acm.2011.0202.

Influence of a specific ginger combination on gastropathy conditions in patients with osteoarthritis of the knee or hip.

Vladimir N. Drozdov, MD, Victoria A. Kim, PhD, Elena V. Tkachenko, MD, and Galina G. Varvanina, MD

Health Care Department, The Central Gastroenterology Scientific Research Institute, Moscow, Russia.

Abstract

Background: Nonsteroid anti-inflammatory drugs represent an important osteoarthritis (OA) therapy component, but also a leading cause of gastropathy: one of the most frequent and serious OA therapy complications. The aim of the present study was to study the influence of GI health in an OA population receiving either ginger or diclofenac.

Methods: Forty-three (43) patients with confirmed OA (knee and hip) were included in a randomized controlled study. A ginger group of 21 patients (17 women, 4 men) was given a specific ginger combination daily (340 mg EV.EXT 35 Zingiber officinalis extract) for 4 weeks. A diclofenac group (positive control) of 22 patients (18 women, 4 men) received 100 mg diclofenac daily for the same period. Both groups also received 1000 mg glucosamine daily. Gastrointestinal pain and dyspepsia were evaluated according to the severity of dyspepsia assessment (SODA) form. Patients also underwent esophagogastroduodenoscopy (EGDS) including biopsy before and after the treatment. Serum gastrin-17 levels, and stomach mucosa prostaglandins (PG) E1, E2, F2α, and 6-keto PGF1α (PGI2) levels were measured. Arthritic pain was evaluated using the visual analogue scale (VAS) on standing and moving.

Results: The ginger group showed a slight but significantly lowered SODA pain and no change of SODA dyspepsia. EGDS showed significantly increased levels of PGE1, PGE2, and PGF2α in the stomach mucosa. This rise in gastric mucosa PG levels correlated with an increase in serum gastrin-17. On the other hand, the diclofenac group showed increased SODA pain and dyspepsia values with a corresponding significant decrease of stomach mucosa prostaglandins and general negative stomach mucosa degeneration. Both groups showed a relevant and significantly lowered VAS pain both on standing and moving.

Conclusions: The ginger combination is as effective as diclofenac but safer in treating OA, being without effect on the stomach mucosa. The increased mucosal PGs synthesis in the ginger group supports an increased mucosa-protective potential.

Efficacia dell'estratto di zenzero nella riduzione dei sintomi da OA al ginocchio

Arthritis Rheum. 2001 Nov;44(11):2531-8.

Effects of a ginger extract on knee pain in patients with osteoarthritis.

Altman RD1, Marcussen KC.

Abstract

OBJECTIVE:

To evaluate the efficacy and safety of a standardized and highly concentrated extract of 2 ginger species, Zingiber officinale and Alpinia galanga (EV.EXT 77), in patients with osteoarthritis (OA) of the knee.

METHODS:

Two hundred sixty-one patients with OA of the knee and moderate-to-severe pain were enrolled in a randomized, double-blind, placebo-controlled, multicenter, parallel-group, 6-week study. After washout, patients received ginger extract or placebo twice daily, with acetaminophen allowed as rescue medication. The primary efficacy variable was the proportion of responders experiencing a reduction in "knee pain on standing," using an intent-to-treat analysis. A responder was defined by a reduction in pain of > or = 15 mm on a visual analog scale.

RESULTS:

In the 247 evaluable patients, the percentage of responders experiencing a reduction in knee pain on standing was superior in the ginger extract group compared with the control group (63% versus 50%; P = 0.048). Analysis of the secondary efficacy variables revealed a consistently greater response in the ginger extract group compared with the control group, when analyzing mean values: reduction in knee pain on standing (24.5 mm versus 16.4 mm; P = 0.005), reduction in knee pain after walking 50 feet (15.1 mm versus 8.7 mm; P = 0.016), and reduction in the Western Ontario and McMaster Universities osteoarthritis composite index (12.9 mm versus 9.0 mm; P = 0.087). Change in global status and reduction in intake of rescue medication were numerically greater in the ginger extract group. Change in quality of life was equal in the 2 groups. Patients receiving ginger extract experienced more gastrointestinal (GI) adverse events than did the placebo group (59 patients versus 21 patients). GI adverse events were mostly mild.

CONCLUSION:

A highly purified and standardized ginger extract had a statistically significant effect on reducing symptoms of OA of the knee. This effect was moderate. There was a good safety profile, with mostly mild GI adverse events in the ginger extract group.

L'estratto di zenzero migliora l'efficacia del diclofenac in pazienti con l'OA del ginocchio

Indian J Physiol Pharmacol. 2013 Apr-Jun;57(2):177-83.

Efficacy and tolerability of ginger (Zingiber officinale) in patients of osteoarthritis of knee.

Paramdeep G.

Abstract

Osteoarthritis (OA) is a chronic degenerative disorder of synovial joints and a common cause of locomotor disability. NSAIDs are routinely used for symptomatic treatment and are associated with side effects which have led to the increased interest towards alternative treatment options. This study was conducted to evaluate the safety and efficacy of ginger in management of OA. Sixty patients of OA of knee were enrolled in randomized open label study and divided into three groups of 20 each. Group I received tab. Diclofenac 50 mg and cap. placebo, group II received cap. ginger 750 mg and cap. placebo and group III received cap. ginger 750 mg and tab. diclofenac 50 mg. The assessment of efficacy was done at every 2 weeks till 12 weeks, by using Western Ontario and McMaster Universities osteoarthritis (WOMAC) index, Visual Analogue Scale (VAS) and the safety assessment was done by noting adverse events during the study. The analysis of WOMAC score and VAS score in all the three groups showed statistically significant improvement with time in all groups. On comparison among three groups, group III patients who received both ginger and diclofenac showed numerically superior improvement than the individual treatments. There was no statistically significant difference among three groups in case of adverse events. Ginger powder has add-on effect on reducing the symptoms of OA of knee with acceptable safety profile.

Efficacia paragonabile di Ibuprofene e Zenzero sui sintomi dell'OA

Archives of Iranian medicine 08/2005; 8(4).

Comparing the Effects of ginger (Zingiber officinale) extract and ibuprofen on patients with osteoarthritis

Masoud Haghighi, Ali Khalvat, Tayebeh Toliat, Shohreh Jallaei

Abstract

Background: Ginger (Zingiber officinale) extract supplementation has been shown to improve the severity of symptoms and decrease the nonsteroidal antiinflammatory drug (NSAID) requirements in patients with osteoarthritis (OA). Objective: To assess the effects of ginger extract as an alternative to NSAIDs and as a supplement drug in the symptomatic treatment of OA. Methods: Between April and October 2002, 120 outpatients with OA of moderate to severe pain, requiring only the use of NSAIDs, were enrolled into a double-blind, randomized, placebo- controlled clinical trial. These patients were randomized into three groups of 40, including the placebo (PL), ginger extract (GE), and ibuprofen (IBP) groups. After a washout period of one week (week 0), patients received either 30 mg ginger extract in two 500 mg capsules, placebo, or three 400 mg ibuprofen tablets daily for one month. Acetaminophen tablet was prescribed as a rescue analgesic during the study. The clinical assessments included a visual analog scale (VAS) for pain, gelling pain, joint swelling measurement, and joint motion slope measurement. Joint motion slope was measured by goniometry (normal = 130°, limited = 120°, and very limited = 110°). Results: The improvement of symptoms (defined as reduction in the mean change) was superior in the ginger extract and ibuprofen groups than the placebo group. VAS scores and gelling or regressive pain after rising the scores were significantly higher in the PL group than both the GE and IBP groups, a month after the treatment ($P < 0.0001$). However, there was no significant difference in VAS and gelling pain scores between the ginger extract and the ibuprofen groups. Conclusion: Ginger extract and ibuprofen were significantly more effective than the placebo in the symptomatic treatment of OA, while there was no significant difference between the ginger extract and ibuprofen groups in a test for multiple comparison.

BOSWELLIA SERRATA

L'azione inibitrice sull'espressione delle metallo proteasi come meccanismo antinfiammatorio

Antioxidants & Redox Signaling

Regulation of Vascular Responses to Inflammation: Inducible Matrix Metalloproteinase-3 Expression in Human Microvascular Endothelial Cells Is Sensitive to Antiinflammatory Boswellia

Dr. Sashwati Roy - Laboratory of Molecular Medicine, Department of Surgery, The Ohio State University Medical Center, Columbus, OH.

Abstract

Endothelial cells are critical elements in the pathophysiology of inflammation. Tumor necrosis factor (TNF) α potently induces inflammatory responses in endothelial cells. Recently we have examined the genetic basis of the antiinflammatory effects of Boswellia extract (BE) in a system of TNFα-induced gene expression in human microvascular endothelial cells (HMECs). Of the 522 genes induced by TNFα in HMECs, 113 genes were sensitive to BE. BE prevented the TNFα-induced expression of matrix metalloproteinases (MMPs). In the current work, we sought to test the effects of BE on TNFα-inducible MMP expression in HMECs. Acetyl-11-ketobeta- boswellic acid (AKBA) is known to be an active principle in BE. To evaluate the significance of AKBA in the antiinflammatory properties of BE, effects of BE containing either 3% (BE3%) or 30% (BE30%, 5-Loxin®) were compared. Pretreatment of HMECs for 2 days with BE potently prevented TNFα-induced expression and activity of MMP-3, MMP-10, and MMP-12. In vivo, BE protected against experimental arthritis. In all experiments, both in vitro and in vivo, BE30% was more effective than BE3%. In sum, this work lends support to our previous report that BE has potent antiinflammatory properties both in vitro as well as in vivo.

Identificazione dei target che spiegano l'effetto antinfiammatorio della Boswellia, tra cui le 5-lipossigenasi e le elastasi

Current Medicinal Chemistry, Volume 13, Number 28, December 2006

Boswellic Acids: Biological Actions and Molecular Targets

Authors: Poeckel, Daniel; Werz, Oliver

Abstract

Gum resin extracts of Boswellia species have been traditionally applied in folk medicine forcenturies to treat various chronic inflammatory diseases, and experimental data from animal models andstudies with human subjects confirmed the potential of B. spec extracts for the treatment of not onlyinflammation but also of cancer. Analysis of the ingredients of these extracts

revealed that the pentacyclictriterpenes boswellic acids (BAs) possess biological activities and appear to be responsible for the respective pharmacological actions. Approaches in order to elucidate the molecular mechanisms underlying thebiological effects of BAs identified 5-lipoxygenase, human leukocyte elastase, toposiomerase I and II, as wellas IκB kinases as molecular targets of BAs. Moreover, it was shown that depending on the cell type and the structure of the BAs, the compounds differentially interfere with signal transduction pathways including Ca2+-and MAPK signaling in various blood cells, related to functional cellular processes important for inflammatory reactions and tumor growth. This review summarizes the biological actions of BAs on the cellular and molecular level and attempts to put the data into perspective of the beneficial effects manifested in animal studies and trials with human subjects related to inflammation and cancer.

Inibizione di 5-lipossigenasi, citochine ed elastasi alla base dell'attività antinfiammatoria dell'estratto di Boswellia

Planta Med. 2006 Oct;72(12):1100-16.

Boswellic acids in chronic inflammatory diseases.

Ammon HP1.

Abstract

Oleogum resins from BOSWELLIA species are used in traditional medicine in India and African countries for the treatment of a variety of diseases. Animal experiments showed anti-inflammatory activity of the extract. The mechanism of this action is due to some boswellic acids. It is different from that of NSAID and is related to components of the immune system. The most evident action is the inhibition of 5-lipoxygenase. However, other factors such as cytokines (interleukins and TNF-alpha) and the complement system are also candidates. Moreover, leukocyte elastase and oxygen radicals are targets. Clinical studies, so far with pilot character, suggest efficacy in some autoimmune diseases including rheumatoid arthritis, Crohn's disease, ulcerative colitis and bronchial asthma. Side effects are not severe when compared to modern drugs used for the treatment of these diseases.

Efficacia significativa dell'estratto di B. in confronto con placebo, su parametri del dolore ed infiammazione nell'OA del ginocchio (8 settimane)

Phytomedicine. 2003 Jan;10(1):3-7.

Efficacy and tolerability of Boswellia serrata extract in treatment of osteoarthritis of knee--a randomized double blind placebo controlled trial.

Kimmatkar N1, Thawani V, Hingorani L, Khiyani R.

Abstract

Osteoarthritis is a common, chronic, progressive, skeletal, degenerative disorder, which commonly affects the knee joint. Boswellia serrata tree is commonly found in India. The therapeutic value of its gum (guggulu) has been known. It posses good anti-inflammatory, anti-arthritic and analgesic activity. A randomized double blind placebo controlled crossover study was conducted to assess

the efficacy, safety and tolerability of Boswellia serrata Extract (BSE) in 30 patients of osteoarthritis of knee, 15 each receiving active drug or placebo for eight weeks. After the first intervention, washout was given and then the groups were crossed over to receive the opposite intervention for eight weeks. All patients receiving drug treatment reported decrease in knee pain, increased knee flexion and increased walking distance. The frequency of swelling in the knee joint was decreased. Radiologically there was no change. The observed differences between drug treated and placebo being statistically significant, are clinically relevant. BSE was well tolerated by the subjects except for minor gastrointestinal ADRs. BSE is recommended in the patients of osteoarthritis of the knee with possible therapeutic use in other arthritis.

Confronto con un coxib nell'OA del ginocchio (6 mesi); l'estratto di Boswellia agisce più lentamente del coxib, ma l'efficacia si protrae a lungo dopo la cessazione del trattamento

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Open, randomized, controlled clinical trial of Boswellia serrata extract as compared to valdecoxib in osteoarthritis of knee

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Objective: To compare the efficacy, safety and tolerability of Boswellia serrata extract (BSE) in osteoarthritis (OA) knee with valdecoxib, a selective COX-2 inhibitor. Materials and Methods: In a randomized, prospective, open-label, comparative study the efficacy, safety and tolerability of BSE was compared with valdecoxib in 66 patients of OA of knee for six months. The patients were assessed by WOMAC scale at baseline and thereafter at monthly interval till 1 month after drug discontinuation. Antero-posterior radiographs of affected knee joint were taken at baseline and after 6 months. Results: In BSE group the pain, stiffness, difficulty in performing daily activities showed statistically significant improvement with two months of therapy which even lasted till one month after stopping the intervention. In valdecoxib group the statistically significant improvement in all parameters was reported after one month of therapy but the effect persisted only as long as drug therapy continued. Three patients from BSE group and two from valdecoxib group complained of acidity. One patient from BSE group complained of diarrhea and abdominal cramps. Conclusion: BSE showed a slower onset of action but the effect persisted even after stopping therapy while the action of valdecoxib became evident faster but waned rapidly after stopping the treatment.