Aquamin

Marine Minerals for Health

Publication overview

INTRODUCTION

Aquamin™ is a natural, marine-sourced multi-mineral, which is derived from the cytoskeleton of the red algal *Lithothamnion* spp. Over the course of the aquatic plant's life, minerals are accumulated from the seawater, and stored as carbonate salts in the plant. 74 components have been identified in total.

Other than washing and milling, Aquamin is unaltered from the raw material and as such represents a natural multi-mineral material that has FDA GRAS certification and is suitable for many food and supplement applications.

Although numerous anecdotal reports of health benefits associated with consumption of Aquamin existed, no objective research was carried out until Marigot Ltd. undertook to understand exactly how Aquamin could impact human health. Over 15 years, Marigot Ltd. have accumulated a large and growing body of research evaluating Aquamin in work spanning in vitro assays, numerous animal models and human trials. This portfolio of research has been conducted independently, and largely at academic institutions across the world, by investigators that are renowned in their respective fields. All researchers are encouraged to publish their results on Aquamin in peer-reviewed scientific journals. As such, this research can be accessed by all and has withstood critique from peers in the relevant field(s).

Aquamin has been demonstrated to have superior bioavailability than other, commonly available calcium sources and has beneficial effects on bone, inflammation, specifically osteoarthritic conditions, digestive health and cardiovascular health. Future research directions will encompass cognitive health while research in all three established areas is on-going, as we explore each one in more detail.

In May 2016 Marigot Ltd was awarded Ingredient of the Year (Healthy Ageing) at the Nutraingredients awards at Vitafoods, Geneva. This is a recognition of the strong body of scientific trial data that supports Aquamin and the positive contribution that it has made to health.

NutraIngredients Awards
2016 • WINNER

Aquamin is the brand name for a series of products owned and developed by the Marigot Group. If you would like to find out more about Aquamin go to Aquamin.com or contact Marigot as below:

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JN THE JOURNAL OF NUTRITION **2014 Impact Factor** - Journal of Nutrition - 3.875

Slevin MM, Allsopp PJ, Magee PJ, et al. *Supplementation with calcium and short-chain fructo-oligosaccharides affects markers of bone turnover but not bone mineral density in postmenopausal women.* **J Nutr. 2014;144(3):297-304.**

MEDICINE & SCIENCE IN SPORTS & EXERCISE® **2014 Impact Factor -** Medicine and Science in Sports and Exercise - 3.983

Shea KL, Barry DW, Sherk VD, *et al. Calcium supplementation and parathyroid hormone response to vigorous walking in postmenopausal women.* **Med Sci Sports Exerc. 2014;46(10):2007-13.**

Barry DW, Hansen KC, van Pelt RE, et al. *Acute calcium ingestion attenuates exercise-induced disruption of calcium homeostasis.* **Med Sci Sports Exerc. 2011;43(4):617-23.**

Recently, Marigot in conjunction with the University of Ulster undertook a large-scale investigation into mineral supplementation and bone health in post-menopausal women (Slevin et al, 2014). 300 participants in this trial were evaluated over the course of 24 months for changes in bone density and bone turn-over markers. Treatment groups included a placebo group, a group that was treated with Aquamin only and a group that was treated with Aquamin in combination with a short-chain pre-biotic (fructo oligo-saccharide, scFOS). In summary, a reduction in bone mineral density losses over the course of 24 months was reported in women with osteopenia at the outset of the trial who consumed Aquamin in combination with scFOS. Furthermore, a reduction in bone turnover markers was reported in both those women consuming Aquamin only and in those consuming Aquamin plus scFOS. All of these findings are indicative of a favourable bone health profile in the population most at risk of osteoporosis and resulting complications.

Calcium metabolism disruption in elite athletes leading to significant losses in bone mineral density has been highlighted in recent years. Whether Aquamin consumption before and during exercise can offset calcium metabolism disruption associated with exercise has been investigated at the University of Colorado in both elite athletes (Barry et al, 2011) and in post-menopausal women (Shea et al, 2014). Using dampening of serum PTH increases associated with exercise (which will in turn result in bone turnover) as a proxy for calcium absorption, it was demonstrated in both groups that Aquamin consumption in a sports drink before and during exercise can reduce exercise-associated calcium metabolic disruption.

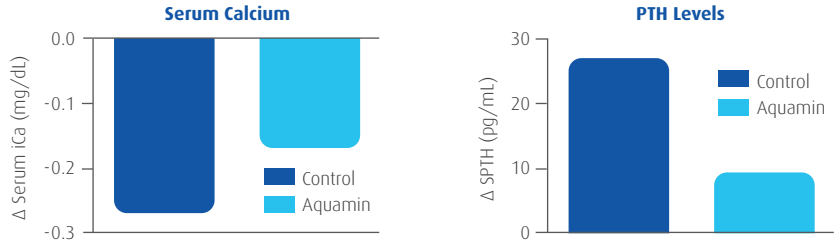

Figure: Shea et al. Changes in Serum Calcium and serum PTH are diminished when Aquamin is consumed (compared to control) in post-menopausal women undergoing a 60-minute brisk walking exercise test.

Investigators at the Royal College of Surgeons, Ireland have demonstrated the ability of Aquamin to improve osteoblast (bone cell) mineralisation both in the absence and in the presence of vitamin D. Using an in vitro osteoblast cell culture technique, those cells cultured in the presence of Aquamin demonstrated a three-fold increase in mineralisation compared to those that were cultured without (O'Gorman et al, 2012). Using the same model, it has been demonstrated that addition of vitamin D to the culture medium increased both ALP levels and mineralisation over that observed with Aquamin alone, and vitamin D alone (Widaa et al, 2014). This work highlights the important relationship between Aquamin and vitamin D, and reinforces the recommendation that Aquamin is consumed along with a diet that is replete in vitamin D. Further support for the role of Aquamin in improving bone growth and osteogenesis was published by the RCSI group in 2015 (Brennan et al, 2015).

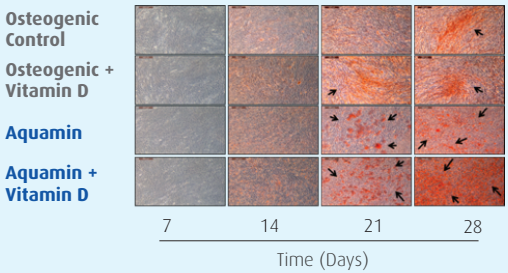

Figure: Widaa et al. Alizarin Red histological staining, which identifies mineralisation by a red stain was examined over 28 days. Aquamin +/_ Vitamin D3 displayed more mineralised nodules than the osteogenic control +/_ Vitamin D3 on days 21 and 28. Aquamin+Vitamin D3 demonstrated the highest quantity of mineralised nodules on day 28, outperforming Aquamin alone.

Researchers at the University of Michigan have investigated the effects of Aquamin in an in vivo model of bone loss – C67BL/6 mice fed a high-fat western diet (HFWD) over time. Aquamin supplementation prevented bone loss and maintained bone strength in mice fed a HFWD, and even resulted in improved bone structure and function compared to mice in the control group (fed a low-fat "healthy" diet) (Aslam et al, 2010). Further investigations using this model revealed a 5 – 10 fold increase in strontium levels in the bones of Aquamin-treated mice, highlighting the synergistic benefit achieved in supplementation with a natural multi-mineral complex as opposed to single source mined material (Aslam et al, 2013).

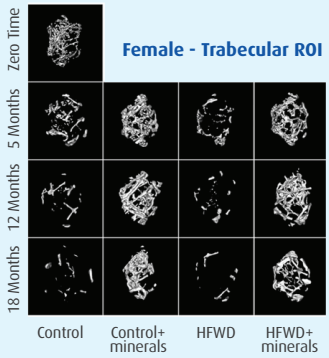

Figure: Aslam et al. µ-CT images: arepresentative 3D µ-CT image of the trabecular region from the femur of a female mouse in each diet group is shown.

Further evidence that minerals besides calcium are important in Aquamin's beneficial effects on bone health was described by Bae et al in 2011 through their use of an ovariectomized (to emulate menopause) rat model. In this work, calcium and magnesium from Aquamin out-performed alternative calcium and magnesium sources with respect to bone density preservation. Using a similar model, it has also been demonstrated that co-adminstration of a probiotic enhanced the performance of Aquamin with respect to bone mineral density (Lee et al, 2010).

NUTRITION JOURNAL **2014 Impact Factor** - Nutrition Journal - 2.6

Frestedt JL, Kuskowski MA, Zenk JL. *A natural seaweed derived mineral supplement (Aquamin F) for knee osteoarthritis: a randomised, placebo controlled pilot study.* **Nutr J. 2009;8:7.**

Frestedt JL, Walsh M, Kuskowski MA, Zenk JL. *A natural mineral supplement provides relief from knee osteoarthritis symptoms: a randomized controlled pilot trial.* **Nutr J. 2008;7:9.**

Initial anecdotal reports of the anti-inflammatory effects of Aquamin were conclusively corroborated in two double-blind, placebo-controlled pilot trials in human patients suffering from knee osteoarthritis performed at the Minnesota Applied Research Centre.

In the first of these trials (Frestedt et al, 2008), 70 subjects with moderate to severe knee osteoarthritis were randomly assigned to one of four 12-week treatment groups. These were 1) glucosamine sulphate (GS), 2) glucosamine sulphate plus Aquamin (G + A), 3) Aquamin (A), 4) placebo (PBO). Patients were assessed using the WOMAC pain score method, and the 6-minute walk test. Patients that consumed Aquamin for the duration of the trial reported less pain in all WOMAC categories, whereas those who consumed glucosamine reported improvement in some symptoms – but not in stiffness. Overall, Aquamin out-performed glucosamine sulphate, and the combination of glucosamine and Aquamin resulted in no significant improvement in pain on the WOMAC score, and was no better than placebo in these parameters. See Figure. Furthermore, 6-minute walk test scores for those patients consuming Aquamin were significantly improved (7%, 101 feet) by the end of the trial, whereas those patients consuming glucosamine sulphate were only able to walk 56 feet further by the end of the trial (see figure) .

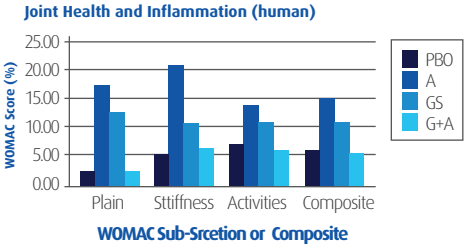

Figure: Aquamin resulted in improved WOMAC scores (i.e. less pain) in all categories.

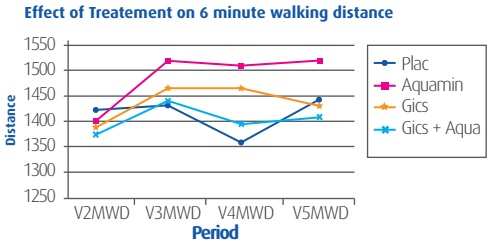

Figure: This demonstrates the improvement in walking distance over a 12 week period on each of the 4 treatments. The most beneficial effects are seen with Aquamin F (pink).

In the second trial (Frestedt et al, 2009), 22 patients with moderate to severe knee osteoarthritis were randomly assigned to one of 2 12-week treatment groups, 1) Aquamin, and 2) Placebo. Patients were assessed while undergoing gradual reductions in non-steroidal anti-inflammatory drug (NSAID) use. At a 50% reduction of NSAID use, patients in the Aquamin group had improved WOMAC pain scores, passive range of joint motion and 6 minute walk test distances compared to the placebo group. While Aquamin is not a pharmaceutical agent, these data indicate that Aquamin may allow partial reductions in NSAID usage in patients with moderate to severe OA.

A third trial performed in Ireland (Murphy et al, 2014) indicated that the addition of pine bark and green tea extract to Aquamin further enhanced the anti-inflammatory effects of Aquamin in knee osteoarthritis, as evidenced by significantly lower serum levels of the inflammatory cytokine TNF-α.

Joint Health and Inflammation (other)

A series of in vitro studies have shed more light on how Aquamin exerts its anti-inflammatory effects in common and debilitating conditions such as osteoarthritis. Production of key pro-inflammatory cytokines including TNF- α and IL-1β are inhibited in the presence of Aquamin and a inflammatory stimulus (LPS) (Ryan et al, 2011). Importantly – the upstream mediator of inflammation, NFκB is also inhibited by Aquamin in a dose-dependent manner, as is the downstream inflammatory mediator most commonly targeted by NSAIDS, COX-2 (O'Gorman et al, 2012).

In support of the findings in Murphy et al, 2014, which examined the combination of Aquamin with other anti-inflammatory compounds, including pine bark, in osteoarthritis patients, the work by O'Callagahan et al, 2013 found that the combination of Aquamin and pine bark extract had both anti-oxidant and anti-apoptotic effects.

Interestingly, recent work has demonstrated the ability of Aquamin to reduce both the incidence and the symptom severity of a severe inflammatory skin disease of mice, ulcerative dermatitis (Hampton et al, 2015).

Digestive Health

Initial observations that cultured gut epithelial (lining) cells demonstrated improved differentiation and regulated proliferation in the presence of Aquamin (Aslam et al, 2009) prompted more detailed investigations into Aquamin's role in digestive health and the role of minerals in regulating gastrointestinal inflammation. When Aquamin was fed to mice being fed a high-fat, so-called "western" diet, it was observed that Aquamin protected mice from colon polyp formation, from generalised GI inflammation and from fatty liver disease (Aslam et al, 2010). This finding was repeated in another trial, in which the amount of calcium was controlled across all groups, but the source was different – mined rock limestone versus Aquamin. Again, despite consuming the same amount of calcium, those mice being fed Aquamin were protected against GI inflammation and resultant polyp formation (Aslam et al, 2012). See Figure. It has also been reported that mice that are prone to developing spontaneous colitis (acute GI inflammation) are less inclined to do so, and experience less severe disease when fed Aquamin, compared to those animals that are not fed Aquamin (Aviello et al, 2014).

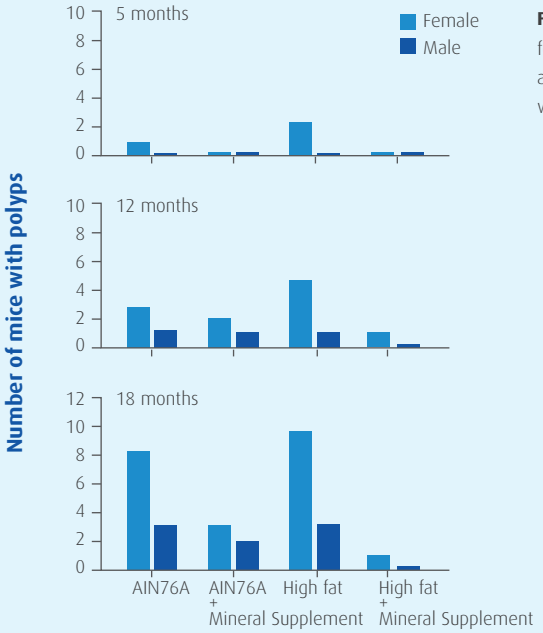

Figure: Colon polyp formation in mice fed Aquamin (mineral supplement) and either a normal or a high-fat western diet.

Taken in concert, these observations have prompted us to investigate along with our colleagues at the University of Michigan, whether these effects on digestive tract inflammation can be observed in humans also – and this trial is currently underway (October 2015).

In an interesting parallel study, it was observed that mice fed Aquamin, whether fed a normal, or a high fat "Western" diet, developed fewer liver masses (Aslam et al, 2012) than those animals that were not fed Aquamin.
These positive effects on GI inflammation are currently being attributed to the calcium sensing receptor (CaSR) that is expressed on the wall of gut lining cells (Singh et al, 2015).

2015 impact factor - British Journal of Nutrition - 3.453

Cronin BE, Allsopp PJ, Slevin MM, Magee PJ, Barbara M Livingstone E, Strain J. J. and McSorley EM. *Effects of supplementation with a calcium-rich marine-derived multi-mineral supplement and short-chain fructo-oligosaccharides on serum lipids in postmenopausal women* **British Journal of Nutrition (2016), 115, 658–665**

Background

Existing evidence on whether calcium supplementation can benefit cardiovascular health (along with known positive effects on bone health) is inconsistent, with some authors reporting a protective effect, and others reporting no benefit, or an increased risk of adverse events. To further investigate this area, cardiovascular health data from 300 post-menopausal women who consumed Aquamin (both with and without scFOS) for 2 years was evaluated and this study contains the results. The publication by Slevin et al (2014) describes the positive effects that Aquamin and Aquamin+scFOS had on delaying bone loss in this at-risk population.

Results

- LDL cholesterol was significantly lower in the Aquamin and the Aquamin+scFOS groups than in the placebo group at the end of the trial, and was maintained within the normal range.
- Total cholesterol was significantly lower in the Aquamin and the Aquamin+scFOS groups than in the placebo group at the end of the trial, and was maintained within the normal range.
- Blood pressure, BMI and body composition were not different between groups.
- IL-4(an anti inflammatory marker)was significantly higher in the Aquamin+scFOS group at the end of the trial.
- Incidence of stroke, heart attack did not differ across groups 4 years after the trial.

This study demonstrates that there is no increased risk of adverse cardiovascular events associated with long-term supplementation of Aquamin.

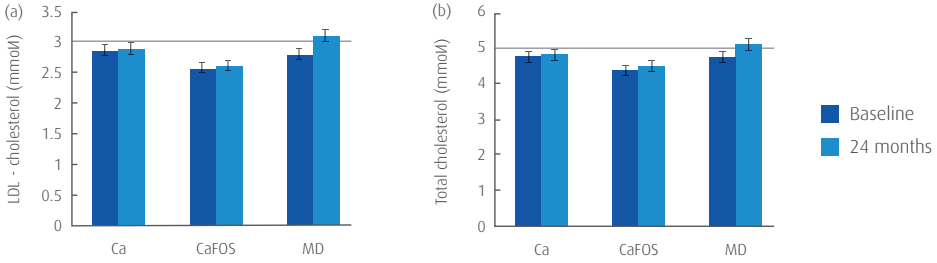

Fig. 2. Effect of Aquamin (Ca), Aquamin and NutraFlora short-chain fructooligosaccharides (CaFOS) and maltodextrin (MD) on LDL and total cholesterol concentrations. Values are means (n 100 in the Ca group, n 99 in the CaFOS group and n 100 in the MD group), with standard errors represented by vertical bars. (a) ANCOVA (with baseline measures as covariates) and least significant difference (LSD) showed a significant treatment effect in the Ca (P=0.02) and CaFOS groups (P<0.01) on LDL-cholesterol over 24 months with reference line to show healthy LDL-cholesterol levels ≤3 ммоИ. (b) ANCOVA (with baseline measures as covariates) and LSD showed a significant treatment effect in the Ca (P=0.02) and CaFOS groups (P<0.01) on total cholesterol over 24 months with reference line to show healthy total cholesterol levels ≤5 ммоИ.

PUBLICATION LIST

BONE HEALTH (HUMAN)

1. **Slevin MM, Allsopp PJ, Magee PJ, et al.** *Supplementation with calcium and short -chain fructo-oligosaccharides affects markers of bone turnover but not bone mineral density in postmenopausal women.* **J Nutr. 2014;144(3):297-304.**
2. **Shea KL, Barry DW, Sherk VD, et al.** *Calcium supplementation and parathyroid hormone response to vigorous walking in postmenopausal women.* **Med Sci Sports Exerc. 2014;46(10):2007-13.**
3. **Barry DW, Hansen KC, van Pelt RE, et al.** *Acute calcium ingestion attenuates exercise-induced disruption of calcium homeostasis.* **Med Sci Sports Exerc. 2011;43(4):617-23.**

BONE HEALTH (OTHER)

1. **Brennan O, Stenson B, Widaa A, et al.** *Incorporation of the natural marine multi-mineral dietary supplement Aquamin enhances osteogenesis and improves the mechanical properties of a collagen-based bone graft substitute.* **J Mech Behav Biomed Mater. 2015;47:114-23.**
2. **Widaa A, Brennan O, O'Gorman DM, O'Brien FJ.** *The osteogenic potential of the marine-derived multi-mineral formula aquamin is enhanced by the presence of vitamin D.* **Phytotherapy research : PTR. 2014;28(5):678-84.**
3. **Aslam MN, Bergin I, Jepsen K, et al.** *Preservation of bone structure and function by Lithothamnion sp. derived minerals.* **Biol Trace Elem Res. 2013;156(1-3):210-20.**
4. **O'Gorman DM, Tierney CM, Brennan O, O'Brien FJ.** *The marine-derived, multi-mineral formula, Aquamin, enhances mineralisation of osteoblast cells in vitro.* **Phytotherapy research : PTR. 2012;26(3):375-80.**
5. **Bae YJ, Bu SY, Kim JY, et al.** *Magnesium supplementation through seaweed calcium extract rather than synthetic magnesium oxide improves femur bone mineral density and strength in ovariectomized rats.* **Biol Trace Elem Res. 2011;144(1-3):992-1002.**
6. **Aslam MN, Kreider JM, Paruchuri T, et al.** *A mineral-rich extract from the red marine algae Lithothamnion calcareum preserves bone structure and function in female mice on a Western-style diet.* **Calcified tissue international. 2010;86(4):313-24.**
7. **Lee HG, Lee TH, Kim JH, et al.** *The effects of a mineral supplement (Aquamin F) and its combination with multi-species lactic acid bacteria (LAB) on bone accretion in an ovariectomized rat model.* **J Exp Biomed Sci. 2010;16(4):213-220**

JOINT AND INFLAMMATION (HUMAN)

1. **Murphy CT, Martin C, Doolan AM et al.** *The marine-derived, multi-mineral formula AquaPT reduces TNF- α levels in osteoarthritis patients.* **J Nutr Health & Food Sci. 2014 2(3):1-3**
2. **Frestedt JL, Kuskowski MA, Zenk JL.** *A natural seaweed derived mineral supplement (Aquamin F) for knee osteoarthritis: a randomised, placebo controlled pilot study.* **Nutr J. 2009;8:7.**
3. **Frestedt JL, Walsh M, Kuskowski MA, Zenk JL.** *A natural mineral supplement provides relief from knee osteoarthritis symptoms: a randomized controlled pilot trial.* **Nutr J. 2008;7:9.**

JOINT AND INFLAMMATION (OTHER)

1. **Hampton AL, Aslam MN, Naik MK, et al.** *Ulcerative Dermatitis in C57BL/6NCrl Mice on a Low-Fat or High-Fat Diet With or Without a Mineralized Red-Algae Supplement.* **J Am Assoc Lab Anim Sci. 2015;54(5):487-96.**
2. **O'Callaghan YC, Drummond E, O'Gorman DM, O'Brien NM.** *Antioxidant and pro-apoptotic effects of marine-derived, multi-mineral aquamin supplemented with a pine bark extract, Enzogenol, and a green tea extract,* **Sunphenon. J Med Food. 2013;16(10):920-6.**
3. **O'Gorman DM, O'Carroll C, Carmody RJ.** *Evidence that marine-derived, multi-mineral, Aquamin inhibits the NF-kappaB signaling pathway in vitro.* **Phytotherapy research : PTR. 2012;26(4):630-2.**
4. **Ryan S, O'Gorman DM, Nolan YM.** *Evidence that the marine-derived multi-mineral Aquamin has anti-inflammatory effects on cortical glial-enriched cultures.* **Phytotherapy research : PTR. 2011;25(5):765-7.**

DIGESTIVE HEALTH

1. **Singh N, Aslam MN, Varani J, Chakrabarty S.** *Induction of calcium sensing receptor in human colon cancer cells by calcium, vitamin D and aquamin: Promotion of a more differentiated, less malignant and indolent phenotype.* **Mol Carcinog. 2015;54(7):543-53.**
2. **Aviello G, Amu S, Saunders SP, Fallon PG.** *A mineral extract from red algae ameliorates chronic spontaneous colitis in IL-10 deficient mice in a mouse strain dependent manner.* **Phytotherapy research : PTR. 2014;28(2):300-4.**
3. **Aslam MN, Bergin I, Naik M, et al.** *A multi-mineral natural product inhibits liver tumor formation in C57BL/6 mice.* **Biol Trace Elem Res. 2012;147(1-3):267-74.**
4. **Aslam MN, Bergin I, Naik M, et al.** *A multimineral natural product from red marine algae reduces colon polyp formation in C57BL/6 mice.* **Nutr Cancer. 2012;64(7):1020-8.**
5. **Dame MK, Veerapaneni I, Bhagavathula N, et al.** *Human colon tissue in organ culture: calcium and multi-mineral-induced mucosal differentiation.* **In Vitro Cell Dev Biol Anim. 2011;47(1):32-8.**
6. **Aslam MN, Paruchuri T, Bhagavathula N, Varani J.** *A mineral-rich red algae extract inhibits polyp formation and inflammation in the gastrointestinal tract of mice on a high-fat diet.* **Integr Cancer Ther. 2010;9(1):93-9.**
7. **Aslam MN, Bhagavathula N, Paruchuri T, et al.** *Growth-inhibitory effects of a mineralized extract from the red marine algae, Lithothamnion calcareum, on Ca(2+)-sensitive and Ca(2+)-resistant human colon carcinoma cells.* **Cancer Lett. 2009;283(2):186-92.**