



The Healing Effects of Nanomized Chinese Herbal Medicine on Overuseinduced Achilles Tendinopathy

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Tendinopathy

- Tendinopathy is a common clinical problem causing pain, disability and mental stress.
 - Characterized by pain and swelling in and around degenerative tendons.
- Achilles tendon is vulnerable to developing tendinopathy, especially among athletes.
 - Continuous, prolonged and intense functional demands during training and competitions.
- 25% to 30% of tendinopathy were non-athletes.
 - This adversely affects their quality of life.
 - Loss of working days.



Achilles Tendinopathy

- Achilles tendinitis:
 - An inflammatory process with the occurrence of pain and swelling at the tendon.
- Achilles tendinosis:
 - A degenerative process without histological or clinical signs of intratendinous inflammation.
- Overuse is believed to be a major causative factor of tendinopathy
 - Failure of the cell matrix to adapt to repetitive trauma.



Picture from http://www.physiocomestoyou.co.uk

Chinese Herbal Medicine and Its Healing Effects

- Chinese herbal medicine has long been applied in management of soft tissue injuries.
 - Injection of total flavones of *Hippophae rhamnoides* (Shaji) promoted biomechanical strength, collagen deposition and enhanced fibre alignment of healing rat patella tendons (Fu et al, 2005).
 - Topically applied *Panax notoginseng* extract coupled with therapeutic ultrasound improved the strength of repairing rat ligament (Ng et al, 2008).





Hippophae rhamnoides



Panax notoginseng

Hypothesis

- Externally applied nanomized herbal medication will have higher penetration power and promote bioavailability for Achilles tendons.
 - > Better treatment efficacy than non-nanomized medication.

Objective

To investigate the healing effects of a nanomized composite herbal medication extract on overuse-induced Achilles tendinopathy.



Methodology

- Animal model:
 - 32 SD rats (3-month old, female)
 - Randomly assigned into 4 groups (n=8)
 - Cage Control (CC)
 - Exercise control (EX)
 - Normal herb treatment and exercise (HB)
 - Nanomized herb treatment and exercise (NH)
- Overuse-induced Achilles tendinopathy was created in EX, NH and HB rats by an enforced treadmill running protocol:
 - Upper body suspended with body weight bore by hind limbs.
 - Speed at 20m/min.

- 20° decline slope.
- 1 hour per day, 7 days per week for 8 weeks.

Herbal Medication Formula

• 4 herbal ingredients Dipsaci Radix (DR), Rhizoma Notoginseng (RN), Flos Carthami (FC) and Rhizoma Rhei (RR) in the ratio 1:1:1:1



Processing protocol of herbal extract

The herbal paste was prepared by mixing 3.9g of aqueous extract and 0.5g of ethanolic extract in 3.4ml 50% ethanol-water.



Ethanolic extract



Herbal paste

Nanomization of Herbal Extract

Hollow iron oxide nanoparticles (HIONPs) were synthesized by hydrothermal method





Herbal Treatment Protocol

- Both HB and NH groups received herbal treatment on both Achilles tendons for 6 weeks after the running protocol.
 - Application on the skin.
 - Daily treatment.



Topical application of nanomized herbal extract



Herbal paste of normal formula was applied on Achilles tendon

Outcome Measures

- Achilles tendons of rats were harvested after the 6-week treatment period.
- The biomechanical properties of Achilles tendons were measured with
 - Load-relaxation.
 - Linear tensile stiffness.
 - Ultimate tensile strength (UTS).



Data Analysis

- Plots of load against time and load-deformation were generated based on biomechanical data.
 - Load-relaxation:
 - Percentage change in load in 5 minutes.
 - Stiffness:
 - Gradient of the linear portion of the load-deformation curve.
 - UTS:
 - Maximum load before failure.
- Statistical analysis was performed using SPSS version 20
 - One way ANOVA with post-hoc LSD test.
 - Statistical significance was set at p<0.05.



Results

- The synthesized HIONPs exhibited high mono-dispersity.
 - Dark edge and pale center region indicated a hollow core and a solid nanoshell.
 - The average diameter of the hollow iron oxide is 195.5 ± 8.2 nm.
 - The shell thickness was determined as 24.3 \pm 1.7nm.
 - > The HIONPs provided a large surface area and capacity for drug encapsulation.



Thermogravimetric study of herbal extractloaded HIONPs

- The temperature of the thermogravimetric study ranged from 150°C to 550°C.
 - The percentage weight loss calculated was 4.07% for blank HINOPs.
 - The average drug loading efficiency was calculated as $13.13 \pm 0.96\%$.



TGA spectrum of herbal extract



Biomechanical Test

Load-relaxation

The load-relaxation of exercise only group was significantly higher than CC, NH and HB groups.

No difference in load-relaxation existed among NH, HB and CC.



Error Bars: +/- 1 SD



Biomechanical Test

Tensile stiffness

No difference in stiffness existed among all treatment groups.



Error Bars: +/- 1 SD



Biomechanical Test

Ultimate tensile strength

The UTS of EX and HB groups were significantly lower than cage control.

The UTS of NH was significantly higher than exercise only group.

No difference in UTS was observed between NH and cage control.



Error Bars: +/- 1 SD

Discussion

- Achilles tendons of EX group demonstrated features of tendinopathy after 8 weeks of forced downhill treadmill running:
 - Increase in load-relaxation.
 - Decrease in ultimate tensile strength.
- Fibroblasts proliferation and collagen fibers disintegration progress with tendon degeneration.
- Collagen fibers become progressively disorganized with tearing at the microscopic level and associated with
 Deterioration in viscoelastic properties.
 - > Lowering of ultimate tensile strength.



Discussion

- The load-relaxation of EX group was significantly higher than the other 3 groups
 - No difference existed among NH, HB and CC.
- The current herbal formula was beneficial to the viscoelastic performance of the tendon.
- Viscoelasticity of tendons determines the capacity of strain energy stored in tendons as occurs in fast locomotion.
- If a tendon does not exhibit normal viscoelasticity and becomes too compliant, positional control would be hampered thus increasing the risk of injury.



Discussion

- The biomechanical properties of NH group were comparable to those of cage control.
- The UTS of NH, but not HB, was significantly higher than that of EX group.
- The healing efficacy of nanomized herbal extract was more pronounced as compared to normal formula.
- Further investigations on cellularity and histomorphology would provide more comprehensive description on the treatment outcomes.



Conclusion

- The results suggested the present formula improved the healing potential for degenerative Achilles tendon.
- Nanomization of the herbal extract further enhanced the healing effect in terms of biomechanical properties.



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