



Getting Right Down to The Bone

Government funds research into the potential of natural leave extracts in inducing bone regeneration in the fight against osteoporosis



Did you know that osteoporosis is a largely ignored health condition? The “silent disease” occurs without symptoms until it is almost too late when a bone becomes brittle enough to break or fracture without force. According to Code Blue – a digital media that publishes free market approach in the development of patient-centric and community-focused health and social sector – 77 per cent of Malaysian women are living with post-menopausal osteoporosis that are undiagnosed.

The condition weakens the bones to the point where they break easily; often, it affects the hip bone, back bone, and wrists. This can happen over a period of years as the bones start losing strength. This is where research plays an important role in finding ways to regenerate bones, increase bone formation, and decreases bone resorption.

Head of Research Management Unit of the university’s Centre for Research and Graduate Studies, Assoc. Prof. Ts. Dr. Intan Zarina Zainol Abidin aims to make a difference with her research that uses an alternative non-toxic product as the cell’s inducer for bone healing therapy which reduces adverse side effects unto patients.

When bone loss is at a severe stage, and requires treatment, patients usually undergo bone healing therapy which use standard drugs such as bisphosphonate. These can create a number of side effects which include oesophageal ulcer and even bleeding after the administration of drugs within 24 to 70 hours. This occurrence is what urged Dr. Intan and her team of researchers to come up with an alternative course of treatment using natural products.

Her research titled, “Determination of Cellular Mechanism in Bone Regeneration using Natural Stem Cells Inducer from *Piper*

sarmentosum (kaduk) Leave Extracts”, studies the development of bone cells from blood stem cells when induced with kaduk leave extracts. Stem cells are cells that have the ability to divide for indefinite periods of time and are able to induce the development of specific cells.

Kaduk, scientifically known as *Piper sarmentosum*, is largely found in countries with tropical climate. Malaysia, with its fortunate location within the equator, is the perfect place to cultivate this plant within ideal weather and soil conditions. The plant is known for its antioxidant, antiplasmodial, antituberculosis, anti-inflammatory, anticarcinogenic and hypoglycaemic properties. In previous studies, it has been found to possess bone healing properties and was able to increase bone strength in rats as test subjects.

“Past research has found that kaduk leave extract have a lot of medicinal value. However, the mechanism of bone regeneration at the cellular level remains unknown. Our objective with this research is to assess its potential as a non-toxic natural inducer that can transform blood stem cells into osteoblasts,” says Dr. Intan.

Osteoblasts are the bone cells responsible for synthesising bone matrix proteins and minerals during early bone formation, controlling

bone formation and mineralisation throughout life. They are found where new bone formation is occurring.

The results of the study were encouraging as they found that the extracts do indeed transform blood stem cells into osteoblasts which concluded that kaduk leave extracts might be a promising alternative medicine for cell therapy to combat bone diseases such as osteoporosis or even bone repair.

Given the importance of this study, Dr. Intan's research secured a Fundamental Research Grant Scheme (FRGS) award of nearly RM100k from the Ministry of Higher Education.

Her co-researchers include Prof. Ts. Dr. Shahrul Hisham Zainal Ariffin from Universiti Kebangsaan Malaysia, Assoc. Prof. Dr. Zaidah Zainal Ariffin from Universiti Teknologi MARA and Anis Nabilah Johari from Universiti Kebangsaan Malaysia.

Part of their research was also published in high impact journals such as Scientific Reports. The research was also awarded with the Best Oral Paper Award in the 11th Kuala Lumpur International Agriculture Forestry and Plantation Conference.

“Although the results of our research prove that kaduk extracts are indirectly involved in bone formation, there are no studies on whether ingesting these plants directly can help strengthen bones.

These require further clinical research. There are also other studies that are looking into the effect of kaduk leaves on animals suffering from osteoporosis,” adds Dr. Intan. With more research, kaduk extracts can be generated into supplements that will be substantial in replacing toxic products in therapy.

“Not many are aware that the population in Malaysia suffering from bone disease is high. Aside from osteoporosis, patients also suffer from osteopetrosis which is a rare disorder that causes bones to grow abnormally and become overly dense. I believe that we will be able to facilitate the repair process with the help of stem cells and kaduk extract,” said Dr. Intan.

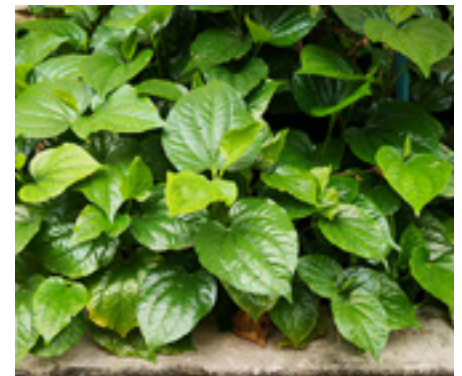
Dr. Intan further explains that her research is merely an *in vitro* experiment (experiments that researchers perform outside of a living organism) that requires more studies before it can qualify for clinical experiments to test on patients.

Studies have shown that bone loss begins from the age of 30-40 and is followed by an immediate decrease in bone mass and density. However, the intake of calcium has a significant effect on bone loss in women. Research has found that calcium supplementation slows the rate of bone loss in postmenopausal women especially those with a low dietary intake of calcium. Moreover, consuming calcium supplements together with vitamin D have also shown to reduce the risk of hip fractures in elderly patients.

However, adults ages 19 through 50 should not get more than 2,500mg calcium in a day, this includes food and supplements, while. Adults over the age of 50 should not exceed 2,000mg in a day. This is because too much calcium in the form of supplements have the potential to increase the risk of kidney stones, constipation, calcium build-up

in blood vessels, and difficulty to absorb iron and zinc.

In conclusion, as our bones support our entire weight, it is important for us to maintain its health. Losing strength in our bones is inevitable as we age, but with the help of calcium, vitamin D, the right nutrition and balanced exercise, the process can be slowed down to a much later stage in life. By then, thanks to the help of new research, better treatment options would be available to treat osteoporosis and other bone diseases sufficiently.



The Kaduk Plant - a non-toxic alternative to bone formation

The wild herb, kaduk or scientifically known as *Piper sarmentosum* and are often confused with betel leaves. Comparatively, kaduk also known as wild pepper, lacks the intense taste of betel leaves and are significantly smaller in size. The plant serves to aid digestion and treat fever in traditional medicine.

Leaves and roots can be placed on the forehead to relieve headache and soup from boiled kaduk water is used to relieve muscle and bone pain. Its leaves may also be pounded and used as a wash to relieve foot fungal itch. The roots of the plant treats ailments such as toothache, coughing, asthma, fungal dermatitis and more.

In fact, the leaves and roots aren't the only parts of the plant that are useful for traditional medicine. Its small fruits help to bring up mucus and other material from the

respiratory tract. The plant's benefits also extend to treating antimalarial effects and anti-clotting action.

A study that was conducted by a team of researchers led by Physiology Medical Lecturer Dr. Nik Aloesnisa Nik Mohd Alwi from Universiti Sains Malaysia in

a popular dish known as otak-otak, which is fish cake made of ground fish mixed in spices.

Osteoporosis - the world's silent disease

The word osteoporosis itself means "porous bone" which creates a condition where the person

Though it is a disease that affects more women than men, the International Osteoporosis Foundation estimate that 1 in 5 men will experience a bone fracture related to osteoporosis in their lifetime. Men who are at a higher risk developing the disease include



Source: <https://www.spineuniverse.com/>

collaboration with other researchers from Universiti Kebangsaan Malaysia found that kaduk leaves decrease high blood pressure among hypertension patients who regularly consumed the dish in their meals. This was due to the antioxidants found within the leaf extracts.

As a Malaysian cuisine, kaduk is used to increase the aroma in cooked meals. They are also eaten raw in nasi ulam, which is a rice salad dish popular within the Malay and Nyonya community. Its raw shoots are dipped in sambal, its flowers are dried as a spice whereas its fragrant leaves are used to wrap fish or meat. This includes wrapping

gradually loses bone material, making their bones gradually more fragile and more likely to break.

As it is a "silent disease", the symptoms are not easily identified until a fracture occurs. However, if there has been a gradual loss of height of 6cm (2.5 inches) from when you were a young adult, you may have had a spinal fracture. Fractures can also lead to persistent lower or upper back pain in the bones and/or muscles.

Other symptoms include developing a stooped posture which causes clothes to not fit properly or having brittle fingernails.

those with unhealthy lifestyle habits such as smoking and having inadequate physical exercise as well as those regularly consuming medications such as glucocorticoids.

Osteoporosis Treatment

Unfortunately, there is no cure for osteoporosis but with treatment, patients will be able to protect and strengthen their bones. Some of the healthcare providers in charge of treating osteoporosis include endocrinologists, geriatricians, gynaecologists, and occupational therapists.

To treat osteoporosis, healthcare

providers find ways to slow or stop bone loss to prevent fractures. These include exercise, increasing the intake of calcium and vitamin D supplements as well as taking medications. Therapy includes using weight and strength-bearing exercises, resistance workouts, and gentle exercises that focus on posture and balance. Those recovering from fractures are medicated with painkillers, or hot or cold treatments to reduce pain.

If patients are currently taking medications that may cause bone loss, doctors would then lower the dose of that medication or switch the patient to another medication. Some medications that help with bone preservation or that help slow down bone loss include bisphosphonates, calcitonin, oestrogen, and hormone therapy, sclerostin inhibitor and more. In men, testosterone therapy helps to increase bone density.

Once patients begin treatment, their bone density may be monitored in either bone density scans or blood and urine tests to show how well the patient's bone is renewing itself. The bone renewal process is a slow one and should be continued to see its results in the long term.

Long term treatment, however, may incur side effects such as irritation to the food pipe, swallowing problems, and stomach pain. Therefore, doctors recommend taking a break from treatment also known as a 'treatment holiday' to recuperate.

History of broken bones and how they are treated in the past and present

Technology advancements have made inefficient orthopaedic treatment more efficient, affordable, quicker, and more effective for the treatment of bones issues. To appreciate this imminent advancement, let's have a look at how broken bones were treated before.

The technique of pouring plaster

of Paris mixture around an injured limb has been used in Arabia for many centuries and was only brought to the attention of European medicine in the 18th century. Arab surgeons used plasters made of mill dust mixed with egg, a mixture of gums, egg white and lime. Plaster of Paris bandages were then introduced by Antonius Methijsen, a military surgeon in Holland back in 1876.

In present times, synthetic casts usually made from a material called fiberglass are used more often than plaster casts. They are more porous and allows doctors to take an x-ray of the injured area without removing the cast. Fiberglass casts also weigh less compared to plaster casts.

Until about 150 years ago, open fractures resulted in either death or immediate limb amputation. Today, open fractures are treated with external fixation which requires doctors to insert metal screws or pins into the bone above and below the fracture site. The pins and screws project out of the skin where they are attached to metal and carbon fibre bars.



Assoc. Prof. Ts. Dr. Intan Zarina Zainol Abidin, Head of Research Management Unit


Upon obtaining her PhD in Universiti Kebangsaan Malaysia, Dr. Intan joined as a post doctorate researcher at its Faculty of Science and Technology with specialisations in Biotechnology (Stem Cell and Cell Biology).

During her time there, she furthered her research in the field of stem cells. Her research interest included the differentiation of stem cells towards other types of cells and the effect of plant extracts on isolated stem cells.

Her research has been published in more than 30 journals including in Web of Science, and Scopus. She has also been appointed as a reviewer by several international and national journals. In 2020, she was awarded as a Professional Technologist by the Malaysia Board of Technologists (MBOT).

She currently acts as the Principal Investigator for an FRGS grant and UoC Research Grant Scheme and is also a co-researcher for several external grants.


Upon 2 years of starting her career in University of Cyberjaya, she managed to secure a Ministry of Higher Education (MOHE) grant to fund her research on the development of bone cells from blood stem cells when induced with kaduk leave extracts. In 2020, she was appointed as a Postgraduate Coordinator involved in postgraduate management in matters pertaining to Malaysian Qualifications Agency (MQA) among others.



More than 1 out of 4 older people (aged 65+) falls each year

X2

Falling once doubles your chances of falling again



1 out of 5 falls causes a serious injury such as broken bones or a head injury

Source: International Osteoporosis Foundation