# **AGING RESEARCH INSTITUTE** NEWSLETTER

## Tabriz University of Medical Sciences (TUOMS)



### **Editorial**

Bone loss in the craniofacial skeleton in geriatric patients

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Age-related bone loss has been little studied in the craniofacial skeleton exceptions of the mandible and the maxilla. Consistent with the importance of the mandible and maxilla in mastication and facial appearance, a lot of studies focus on these bones. However, because of edentulism and periodontal disease, two commonly encountered conditions that can independently cause bone loss, the mandible and maxilla have also proved to be involved in complex situations of aging-associated osteopenia. Tooth loss causes to localized bone loss, for the reason that it eradicates a source of mechanical loading and maybe stem cells and growth factors (in the periodontium) are main in sustaining bone mass, predominantly in the alveolar bone that surrounds the tooth roots.

However, the consensus of most studies is that there is a naturally happening age-related loss of alveolar bone that arises independently of edentulism and periodontal disease. Furthermore, there looks to be a positive association between osteoporosis in the postcranial skeleton and the osteopenia that happens in the alveolus [1]. Wactawski-Wende et al. [2] compared the risk (odds ratio; OR) of loss of alveolar bone with the severity of loss in bone mineral density in another place in the body. The data display that the greater the systemic osteoporosis, the higher the risk of alveolar bone loss. For example, after adjustment for different co-factors containing age, weight, hormone use and education, the OR for alveolar crest bone loss for an osteoporotic woman (T score <-2.5) aging 70 years or older is about 3.6[2].

As stated by a correlation between the degree of systemic osteopenia or osteoporosis and the loss of alveolar bone, it is not surprising that hormone replacement therapy (HRT) is efficient in curtailing bone loss in both circumstances.

In a double-blinded, placebo controlled trial done by Civitelli et al. [3] postmenopausal women with no evidence of moderate or severe periodontal disease were treated with conjugated oestrogen (alone or in combination with medroxyprogesterone) or placebo, and were followed for three years. The results displayed that HRT increased alveolar bone mass and perhaps height in parallel with increases in postcranial bone density in the femur. As noted above, although oral bone loss arises in most individuals as a part [Cont.]

We are delighted to offer our sincerest congratulations to our valued Christian colleagues and followers of Jesus Christ, the prophet of peace and kindness, on new year. We hope that the coming year will be full of success, prosperity, and peace for all nations. We wish you a year full of happiness and health. Нарру 2020.



Sketch: Ali Shamekh, Medical Student of TUOMS

#### **Biography: Prof. Soodabeh Davaran**



Professor Soodabeh Davaran was born in 1965 in Tabriz, Iran. She received her PhD in Polymer Chemistry (Pharmaceutical Biomaterial) in 1996 from Tabriz University and getting her professor rank in chemistry department in 2008 from the Faculty of Pharmacy at the Tabriz University of Medical Sciences (TUOMS). At present, she is the head of nanomedicine department in the School Of Advanced Medical Sciences, TUOMS. Professor Davaran has published about 200 papers in international journals. She has also registered 15 national patents in the field of novel drug delivery systems and nanomedicine. She has supervised more than 60 thesis in the field of pharmacy, nanotechnology, and biomaterial. She has the highest h index among the female academic staff in the northwest of Iran. The fields of her research include biomaterial development for drug delivery systems in particular anticancer therapies and tissue engineering especially skin, bone, and cartilage.

She has been involved in the establishment of two research center and set up of three laboratories at Medical Institute of Tabriz University of Medical Sciences. At present, she is the head of nanomedicine department in the Faculty of Advanced Medical Sciences. She is the advisor of the East Azerbaijan Province Governor-General in research and development of women's affairs. In recent years, she has been awarded several prizes. She is also a member of the editorial board of three scientific journals and a member of the American Chemical Society. Some of her national and international achievements are as follows:

### Message

Dear colleagues and friends at the Alavi center in Tabriz!



As we pass the winter solstice and enter the last days of 2019, I feel an urge to talk about the loss of the real world and its replacement with a virtual world. The advent of the internet and the subsequent introduction of social media, along with the loss of written books and printed papers, contributed to the plunge of humanity into an artificial world that exists only in people's heads and in the computers where the digitized instructions reside with little similarity to or affinity with the world that they mimic. If visitors from an alien world were to come upon the earth at a time in the future when all computers and networks had been turned off, as in The Second Sleep, they would have no chance to imagine the images that these machines once invoked in the observers of the screens and pads and readers when the devices were active. The interesting question is whether the visiting aliens would be able to make sense of the instructions and feed them accurately to the machines that they had somehow managed somehow to turn on.

The dilemma reminds me of the issue of what the world would be like if humans or other potential observers were not there to interpret the signals. Even the question itself of what it would be "like" would be meaningless if no one were present to interpret the signals. This may happen in the future but has not happened yet. Fortunately, there is still time during the current turning of the wheel of years to safely indulge in the admiration of the world itself and ponder these philosophical questions, even without the aid of internet and networks and social media, other than those our brains are equipped with, courtesy of the generosity of evolution and Nature, whomever she or he or it is.

The word "wheel" of the wheel of years is "hjul" in Danish that also gave rise to the word "jul" for solstice or "Yule" in English, a word that is equally useful to all inhabitants of the world, regardless of which of the many past, present or future events and changes at the times of the solstices we focus on as individuals or as members of diverse groups. As such, jul or Yule refers to the general solstice, whether Winter or Summer, depending on where you live. It is everywhere the season for giving and receiving and remembering, unaided by mindless computers, and bringing to mind the togetherness that we as humankind depend on. Therefore, this letter is for you! May you all enjoy a merry yuletide and a happy new turn of the wheel!

• The UNESCO Medal for development of Nanosciences and Nanotechnologies.

 First rank in National Razi Festival in Basic Sciences among more than 60 universities of medical sciences.

Entitled as "Women Elites of Iran and All Elites around the Islamic World".

· Selected as "The world's top scientist by International biographical canter of Cambridge".

• Top Researcher in Tabriz University of Medical Sciences.

Prof. Albert Gjedde



#### Editorial [cont.]

of the aging process, the loss of teeth remains a very significant factor in determining the extent and location of oral osteopenia. After the loss of teeth, there is an accelerated resorption of residual alveolar bone that keep on for numerous months followed by a slower rate of localized osteopenia that may continue for many years, even in the existence of dentures. The loss in the mandible is about four times greater than that detected in the maxilla [4-6]. Presently, the best

method for maintaining alveolar bone seems to be the dental implant, provided that the associated restoration lets for balanced occlusal loading on mastication and that following care controls periodontal disease at the implant site.

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The iHAN organization committee for-

mally met for the first time in 2009 to in-

itiate collaboration between researchers

in Denmark, Singapore and Australia,

which expanded to include researchers

from other universities. The Network

meets 4 times a year, often in groups of

the individual nodes and professor Al-

bert Gjedde, a Danish-Canadian neuro-

scientist and Professor of Neurophysiol-

ogy and Pharmacology at the Faculty of

Health Sciences and Center of Neurosci-

ence at the University of Copenhagen, is

Researchers of iHAN include members

Universities of California, yale, johns

Hopkins, Queensland, van Stellenbosch,

McGill, British Columbia, Aarhus Univer-

sity, Copenhagen, Oslo and fortunately

since 2015, Tabriz University of Medical

Sciences has joined the network affiliat-

ed with the University of Copenhagen by

the head of the iHAN network.

from:

(iHAN)'s interaction with IARU:

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Aging Research Institute including Neu-

its Aging Research Institute.

#### International Healthy Aging Network (iHAN)

The International Alliance of Research Universities (IARU), established in 2006, is a network of eleven international research-intensive universities from nine countries across the globe.

The eleven members share similar values, a global vision and a commitment to educating future world leaders. Central to these values is the importance of academic diversity and international collaboration as reflected in IARU's principles. The IARU Members are the Australian National University, ETH Zurich, National University of Singapore, Peking University, University of California, Berkeley, University of Cambridge, University of Cape Town, University of Copenhagen, University of Oxford, the University of Tokyo and Yale University.

The Chair of IARU is Dr. Makoto Gonokami, the President of the University of Tokyo. The IARU Secretariat is also located at the University of Tokyo.

International Healthy Aging Network

#### Mini Review

#### Melatonin and age-related disease

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#### Abstract

Aging process leads to different consequences including losing the function of various tissues, and increasing the possibility of several disease occurrence. However, the exact mechanism of aging remains unknown, but reactive specious accumulation and activation of different inflammation pathways are among the most possible mechanisms of aging. Melatonin is a pleiotropic hormone. Previous studies showed that melatonin act as an anti-oxidative and anti-inflammatory agent. Also, various studies showed that melatonin is capable to reduce the negative effects of aging. In this study, we will discuss the mechanisms of aging and melatonin on the body by having a look at previous researches.

sized from tryptophan [6],[7]. Melatonin has a wide distribution within highly developed creatures to very simple organisms [7]. Melatonin is the main product of pineal gland and has the role of controlling the circadian and circannual [6],[7]. melatonin exists in many extra pineal tissues and organs independently of the pineal gland including: the retina, thymus, thyroid, stomach, gastrointestinal tract, airway epithelium, liver, spleen, pancreas, heart, skeletal muscle, placenta, testes, ovaries, cerebral cortex, kidney, adrenals[6], skin, platelets and bone marrow [7]. Melatonin acts as a multitasking molecule by having antioxidant, oncostatic, antiaging, and immunomodulatory effects [8]. It also prevents cells from oxidative and inflammatory damage [6].

Following is a detailed mechanism of aging and melatonin's protective role on them.

## Inflammation and oxidative stress in aging

The inflammatory process which is associated with aging is called inflammaging [9]. However the exact mechanism of inflammaging remains unknown, but it is possible that dysregulation of the cytokine network and its homeostasis plays a critical role in inflammaging. previous studies indicated that several common molecular pathways are associated with aging and low-grade inflammation [2]. The main role of inflammation is to restore the physiological homeostatic state [9]. Several stimuli trigger inflammation, including DNA damage [2], metabolic stress, pathogens, or injury [9]. Aging process cause impairment in the cell machinery process that removes damaged proteins and large aggregates which is the characteristic of age-related diseases. all these factors lead to NF-κB and the IL-1β- mediated inflammatory cascade [2]. Activation of NLRP3 inflammasome-related innate immunity rosciences Research Center, Research Center of Psychiatry and Behavioral Sciences, and Physical Medicine and Rehabilitation Research Center has been established in Tabriz University of Medical Science (TUOMS) in 2016 in honor of professor Abass Alavi for the his indefatigable and resolution to advance aging studies. The head of the institute is Prof. Seyed Kazem Shakouri. This institute actually tries to promote national understandings about aging processes by implementation of national and international scientific capabilities and cooperation with other global and distinguished centers of science.

Peyman Keyhanvar, MD, MBA, Fellowship of Technology, who is PhD in Medical Nanotechnology and Regenerative Medicine, is acting as Head of TUOMS iHAN branch and is in charge of organizing iHAN, under supervision of the insti-

pathways amplifies the inflammatory

response NF-KB mediated. Once the in-

flammasome is activated, caspase-1 ad-

vances pro-IL-1β and pro-IL-18 into their

mature active process and induce their

subsequent secretion. Finally, IL-1ß and

IL-18 initiate an inflammatory process of

regulated cell death known as pyropto-

sis [9]. One of the other characteristics

is increased oxidative stress causes the

accumulation of reactive oxygen spe-

cies and reactive nitrogen species [10].

It has been proved that iNOS expression in aged rats is higher than young rats

[11]. Nitrite levels is a sign to indicate

the nitrosative stress status, which is

caused by inflammation [12]. The con-

temporary increase in lipid peroxidation and oxidation of mitochondrial proteins

increase the oxidative stress effects. As

a result, differential accumulation of oxi-

dative damage occurs, which can cause

impairment of different tissues in the ag-

Melatonin and its anti-aging capability

In addition to neural and cardiovascular

systems as well as the liver and ovary,

ing process [10].

tute head Prof. Seyyed Kazem Shakouri and the main aim of this branch is to play as an organization in 3rd generation universities focusing on converging knowledge and technologies (NBICS) and entrepreneurship aims especially startups. Suggested programs of TUOMS branch of iHAN are :

cranial bone density in postmenopausal women re-

ceiving hormone/estrogen replacement therapy: a

randomized, double-blind, placebo-controlled trial.

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- 1- Developing the Aging Network
- 2- New international Interdisciplinary Course
- 3- Networking in in-silico Aging
- 4- Developing Startups Accelerator
- These programs will explain more in the next issues
- iHAN has also started its activities on social networks, including Instagram with @ihan\_tbzmed ID. The content of the Instagram page contains material to acquaintance with iHAN and IARU, introducing members, video report of meetings and the pioneers of this field. Sara Mohammadzadeh, Shadi Farabi

in the field [7]. It is known that melatonin and so as its metabolites remove reactive oxygen species (ROS) and reactive nitrogen species (RNS) [13]. Other studies showed that melatonin and its metabolites regulate a variety of molecular pathways such as proliferation, apoptosis, and metastasis in different pathophysiological situations [13],[7]. Studies showed the presence of melatonin receptors in numerous tissues has led to great discoveries of the antioxidant and anti-inflammatory properties of melatonin [6]. The production of reactive oxygen (ROS) and reactive nitrogen species (RNS) takes place mainly during the phases of the metabolic, motor, and neural activity, when oxygen consumption is maximal; these activities do not necessarily occur at night in diurnal animals. Thus, melatonin may be produced in non-pineal cells as a protective mechanism against the metabolites of aerobic metabolism [6].

## Melatonin and its protective effects on age-related disease

Previous researches indicated that age-dependent nitrosative status in brain mitochondria was prevented by melatonin administration [12]. Variety of studies have demonstrated that melatonin can act as an anti-oxidant and anti-inflammatory agent in different age-related disorders. Mitochondria [Cont.]

#### Introduction

Aging is a complicated process associated with many different factors which lead to damaged cells and tissues resulting in losing function and increasing the risk of a wide range of disease [1]. Aging causes different abnormalities in cell homeostasis. abnormal inflammation pathways are among the most probable causes in age-related disease such as cardiovascular disease, diabetes, metabolic syndrome[2], osteoarthritis [3], neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Amyotrophic Lateral Sclerosis (ALS), Huntington's disease [4]. Defected inflammation pathways also cause a different type of cancer, and aging itself [2]. Melatonin (N-acetyl-5-methoxy-

tryptamine) is an endogenous molecule [5]. Biosynthesis melatonin is synthemelatonin has documented anti-ageing potential in the other organs as well (Fig. 1)(11). Melatonin has been shown to play a critical role in skin functions including hair cycling and fur pigmentation. Melatonin uses four echanisms to function, including 1) interaction with membrane receptors, 2) binding to nuclear receptors, 3) interaction with cytoplasmic proteins and 4) via direct, receptor-independent actions[8]. Melatonin's anti-oxidative action is associated with increasing the levels of several anti-oxidative enzymes including superoxide dismutase, glutathione peroxidase and glutathione reductase [13],[7]. Melatonin is a potent free radical scavenger, more potent than vitamin E, which is the reference

#### **Top Article**

Congratulations to Mrs. Somaiyeh Taheri-Targhi, MSc in history of medicine, TUOMS, on having her article entitled: "Avicenna (980–1037 CE) and his Early Description and Classification of Dementia", published in Journal of Alzheimer's Disease, (IF=3.51) which has been selected as the top article of this issue. Aging Research Institute expresses the warmest greeting to her.

#### Mini Review [cont.]



Fig. 1. The anti-ageing potential of melatonin on different organs.

contribute to aging process By production of Reactive Oxygen Species (ROS) [11] and involve in the oxidative and inflammatory process by reducing their effects [14]. Observations in cells that are undergoing the aging process showed that there was an alteration in the expression and activities of the antioxidant enzymes in response to the oxidative environment [15]. Melatonin treatment of the cells which were under an aging process showed that melatonin could alter the situation by its anti-oxidative role [11]. Melatonin prevents the rise in mitochondrial LPO and increased GPx and GR activities, and leads to normalizing the GSSG/GSH ratio [16]. Melatonin has been reported to protect the mitochondria by preventing cardiolipin oxidation. Consequently, melatonin could promote the mitochondrial transition pore opening (MPTP), resulting in cell death [17].

Different studies indicated that some age-related disease is also related to melatonin's level in those patients. Studies showed that by the onset of puberty the melatonin's secretion starts to decrease. Insofar as by the middle age, this reduction in melatonin level leads to neurodegenerative disease. Alzheimer's disease or AD is one of the most prevalent neurodegenerative diseases in old people. Neurological markers of AD begin to develop after puberty which is the same time as when melatonin levels start to reduce. Neurodegeneration in AD is also a company by decreased receptors of melatonin in the pineal gland and the areas which are involved by AD [18]. Previous researches indicated that melatonin exerts protective effects against ischemia-reperfusion injury in various the heart. A study showed that administration of melatonin plus standard treatment significantly reduced the level of creatine kinase-MB in myocardial infarction patients. In another study, melatonin could protect CIH-induced myocardial inflammation, fibrosis, and ischemia-reperfusion injury by reducing the expression of inflammatory cytokines including (TNF-a) and IL-6, markers of fibrosis such as (TGFb) [19]. It has been reported that melatonin has chondroprotective effects [20]. Melatonin stimulates extracellular matrix synthesis of porcine articular chondrocytes in serum-containing pellet culture system through the TGF-b signaling pathway [5]. Furthermore, according to a study, the anti-arthritic effect of melatonin via inhibition of IL-1b- and TNF-ainduced intracellular ROS accumulation and MMPs production in vitro have been reported [20].

to a wide range of disease. Melatonin is known as a powerful anti-inflammatory[6] and anti-oxidant agent [7]. Different studies indicated that melatonin is capable to alleviate unfavorable effects of the aging process such as neurodegenerative disease[4], cardiovascular disease[19], osteoarthritis[3], etc. Considering this review paper it is crucial to plot further studies to gain more information about the probable role of melatonin in the alleviation of age-related disease.

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### **Student Letter**

#### **Elder Abuse**

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In each society, older adults aged over 65 are the most vulnerable groups more likely to be exposed to abuse while receiving supportive care. Elder abuse can diminish self-confidence, make feelings of hopelessness and apathy, and cause psychological disability in the elderly[1-3]. The best definition of elder abuse is a harmful action by a person who the elder trust. [4]. According to some sociologists and health professionals, societies are increasingly facing elderly maltreatment, which includes physical ,sexual, psychological, emotional and financial abuse; negligence and abandonment[5, 6]. Of course, one form of abuse can easily lead to another, for instance when an elderly person is asked for money, the refusal of this request causes another physical abuse. Individuals that impose elder abuse have a wide variety. they can be a caretaker, family member, or stranger[4].

Most of the harm that is common to older people appears to be psychological violence, including persistent verbal disrespect, harassments, threats, physical and financial deprivation. Studies have shown that the types of elder abuse in Iran are more prevalent than in Western countries and Compared to other provinces East Azerbaijan has less abuse prevalence than any other regions of Iran. The first and main step towards addressing the risk of elder abuse is familiarity with the concepts of elder abuse and its indicators [7].

There are six types of elder abuse that their indicators are as follows:

#### 1. Physical abuse:

 Multiple fractures or injuries in various periods of healing

 Bruises gathered together and in regular forms, especially in unusual locations such as the neck or groin.

 Lashes from a belt can cause injuries extending over several regions, such as the front, side, and back of the legs

 Patterned injuries that can give clues to the size and the shape of the object that caused them, such as belt buckles or hands

#### 2. Sexual abuse:

· Injuries to the chest, abdomen, genitalia, buttocks, and upper thighs, which may suggest a sexual abuse

 Forced sexual activity can cause noticeable injuries, pain, or itching in the genital region; evidence of sexually transmitted diseases; and broken teeth 3.Nealect:

- Anxiety about personal finances
- Pressure by someone else to endorse checks
- 6. Abandonment:
- Leaving elderly alone or cessation of providing care

Personal issues can also cause someone to become an abuser. Personal issues like money, bills, or health problems can affect the caregivers's work and cause abuse.

There are 10 steps to take when you think abuse is happening:

1.Recognize the type of elder abuse 2.Look for elder abuse signs

3.Talk with the elder person (Some elder people will deny when they are being abused. This is particularly true when it is a family member causing the abuse. You should still report even if they deny the abuse)

4. Talk to the elder family

5.Report the abuse

6.Wait is the next step (The adult protective services will start an investigation and might assign a case manager)

7.Now the next step is to prevent any more abuse (Look for risk factors of abuse)

8.Speak to the elder and the caregiver. By visiting and calling more often, you can get a better sense of what is happening in the environment. 9.Protect yourself

10.If you are a caregiver and feel angry with your caregiving job, ask for help; so you are not abusing whom you are supposed to be taking care of.[4, 8]

It is mandatory for everyone to report abuse however it is rarely done. If you see any type of elder abuse happening, please report it by calling 123.

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#### Conclusion

The aging process is responsible for several severe age-related diseases in an old population of a society. Inflammaging[9] and accumulation of reactive specious[6] as a result of aging, leads

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- Deterioration of health
- Dehydration, malnutrition, or cachexia
- Inappropriate clothing

 Assistive devices missing or in poor repair, such as broken glasses

Urine burns

- 4. Emotional abuse:
- Paranoia, depression, or anger

Fear of strangers

- Exhibiting fear in own environment
- Low self-confidence
- 5. Financial abuse:
- · Lack of sufficient food and medications

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#### Volume 2/ Issue 1

#### International Project (No.5)

Ginger (Zingiber officinale) and turmeric supplementation effects on quality of life, bone mass densitometry (BMD), body composition and osteoporosis related biomarkers and micro-RNAs in women with postmenopausal osteoporosis

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Our international project, entitled as "The Effect of Ginger and Turmeric on postmenopausal osteoporosis" evaluates ginger (Zingiber officinale) and turmeric supplementation effects on quality of life, bone mass densitometry (BMD), body composition and osteoporosis related biomarkers and micro-RNAs in women with postmenopausal osteoporosis.

This study is a randomized controlled double-blinded clinical trial with placebo that aims to investigate the effects of ginger (Zingiber officinale) and turmeric supplements alone or in combination with each other in postmenopausal osteoporosis women which has been trialed by Hanieh Kheiridoost, as the student of this project, and Seyed Kazem Shakouri and Neda Dolatkhah. from Tabriz and Anne Pernille Hermann from Denmark as the principle supervisors.



After selecting survey respondents and explaining the methods and goals of the project and obtaining informed consent, patients were randomly assigned to receive the treatment for 4 months as follows: 1)Ginger supplement (one capsule containing 1000 mg daily) 2)Turmeric supplement (two capsules containing 500 mg daily) 3)Ginger-Turmeric supplements 4)Placebo

The inclusion criteria were women with natural menopause, aging 45 years and older, cessation of menstruation for 12 consecutive months, low bone density, no history of fractures, non-hormone treated during the past six months, no steroid use over the past six months, no infection and kidney failure, no metastatic bone disease, no medication affecting bone metabolism other than calcium supplements that will be administered to all study respondents with the same dose, no mental disease, no malignancy, non-use of walking aids and the ability to communicate verbally and respond to questions. Use of birth control pills or steroids during the study, the risk of kidney failure during the study and not wanting to continue the study were the exclusion criteria.

To explain about the sample size, we can say that due to the lack of similar studies in the literature review, a pilot study evaluated 25 patients in each group will be done to get the power of 0.8 and a Type I error equal to 0.05. If the power of study with his sample size is close to 0.8, the sampling would be stopped and otherwise, sampling will be continued more to obtain the power of 0.8. Interventions in this study are 1-Ginger; 2- Turmeric; 3-Turmeric and Ginger and 4-Placebo which have been intervened on patients for 4 months.

Whereupon the primary outcomes are evaluating the ginger (Zingiber officinal) and turmeric supplementation effects on the quality of life, bone mass densitometry (BMD), body composition and osteoporosis related biomarkers and micro-RNAs. And secondary outcomes are followed as the dietary intake of macronutrients and micronutrients in postmenopausal women in all four study groups and comparison with RDA (Recommended Dietary Allowance).

Talking of potential relevance and clinical impact of our study in women's life is that is mentioned these days in the medical world, one of the goals of "Health for All in the 21st Century" is to promote the quality of life. Given the principle that older women are a valuable and important part of the human resources of the community and their health in the post-menopausal age is as important as before menopause, and also considering the cost-effectiveness of using the plant compounds in comparison with pharmaceutical compounds, we decided to evaluate the effect of turmeric and ginger supplements alone and also in combination on quality of life, body composition and osteoporosis related biomarkers and micro-RNAs in postmenopausal women suffering osteoporosis.

Based on our knowledge, there has not been performed any clinical trial with

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this goal ever. Data will be presented as mean (± SD) and frequency (percentages) for qualitative and quantitative variables respectively. Normal distribution of data will be assessed using the Kolmogorov-Smirnov test.

The parametric tests will be used for normally distributed variables and for variables with non-normal distribution, nonparametric tests will be used. According to the correlation between the variables studied, to compare the characteristics and basic measurements of biochemical variables between the patients into four groups and at different times, the Mixed ANOVA statistical methods will be used. ANCOVA statistical method will be used for the effect of confounding variables on the response variables. The p-value of less than 0.05 will be considered significant. The time scheduled for this study was about 20 months and the budget used was 5500 USD.

The compassion and efforts of Professor Hassan Soleimanpour, former Research Vice Chancellor and Editor-in-Chief of the Aging **Research Institute Newsletter, are** commendable in conveying his valuable scientific experiences. This honorable man's responsibility and devotional abilities merits an appreciation in this field. Hereby, the staff of Aging Research Institute and the Editorial Board of the Newsletter would like to express their gratitude and appreciation for his valuable and sincerely efforts.

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17 6

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4

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