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# Biochem Trends

## Newsletter

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# Turn the pages to discover




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# Editorial

## Biochemistry : Evolving through the ages

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Biochemistry is a science that spans over many areas and has its essence infused in most aspect of medicine and biology.

The term "biochemistry" was christened by Carl Neuber in 1903 (*Singh P, Batra HS, Naithani M. History of biochemistry. Bulletin of the Indian institute of History of Medicine (Hyderabad). 2004 Jan-Jun;34(1):75-86. PMID: 17152615.)*, however, biochemistry came in to being long before its naming ceremony.

Several study areas are coined under 'biochemistry', these include neurochemistry, bioorganic chemistry, clinical biochemistry, physical biochemistry, molecular genetics, biochemical pharmacology, and immunochemistry. The list goes on. Yet going to the very beginning biochemistry started off with the elucidation of chemistry of fats, proteins, and carbohydrates

It looks at the molecular level of life. Initial discoveries investigated the basic building blocks of these macronutrients and how they functioned, their involvement in keeping us healthy. With time we identified the role of biochemistry and its involvement in disease. Today biochemistry is reaching far and wide and not just looking into the physical wellbeing of a person and/or society but also the emotional wellbeing. New discovers, new branches of biochemistry are being discovered and will continue to be discovered. We are expanding, we are evolving, and the future is promising, the day when biochemistry has itself involved in all of science is fast approaching, if not already here.

This newsletter looks in to three articles, that portray the expansion of biochemistry in to new and varying areas of study.

What vitamin D does in lumbar disc disease.

Heat shock proteins in diabetes mellitus:  Role and targeting

Molecules of emotion; the new science of psycho-neurochemistry

While looking into the future, we also need to take a glimpse in to our history. Remember the path once trodden, acknowledge the work of our forefathers and appreciate their role in bringing us to the here and now. What we know today was discovered painstakingly over a number of years. What we know tomorrow is what we are discovering now.

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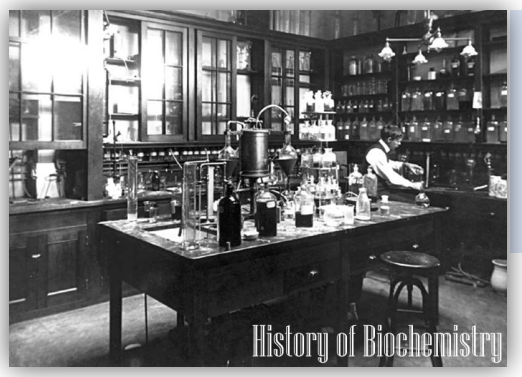



# Biochemistry History - A timeline

*https://www.bioexplorer.net/history_of_biology/biochemistry/*

| | |
|---|---|
| **17th Century** | |
| 1665 | Robert Hooke invented the microscope |
| 1674 | Anton van Leeuwenhoek witnessed a live cell (plant) under a microscope |
| **18th Century** | |
| 1775 | Antoine Lavoisier : proposed a mechanism for photosynthesis and investigated cell respiration in animals |
| 1777 - 83 | Hypothetical principle of fire<br>The onset of physiological chemistry (i.e chemistry of digestion and of body fluids) |
| **19th Century** | |
| 1839 | Cell theory, Theodor Schwann |
| 1856 | Louis Pasteur opposed Liebig's chemical theory |
| 1860 | View that the protoplasm carries out all the intracellular processes. |
| 1869 | Friedrich Miescher first identified what he called "nuclein" inside the nuclei of human white blood cells |
| **20th Century** | |
| 1900s | Eduard Buchner - Cell free fermentation, and the role of the "enzyme" |
| 1904 | The term "biochemistry" was officially coined by the German chemist Carl Neuber. |
| 1919 | Phoebus Levene, discovered the order of the three major components of a single nucleotide (phosphate, pentose sugar, and nitrogenous base). Discovered the carbohydrate component of RNA (ribose) and DNA (deoxyribose). |

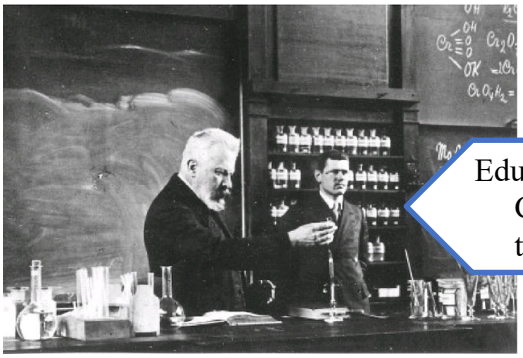
## Biochemistry History – A timeline, contd…..

| | |
|---|---|
| 1937 | Hans Krebs discovered the process of the Citric Acid Cycle (Krebs cycle) |
| 1944 | Oswald Avery suggested that the genetic material of the cell was possibly the deoxyribonucleic acid. |
| 1950 | Erwin Chargaff concluded that almost all DNA, maintain certain properties, even as its composition varies. "Chargaff's Rule", the amount of pyrimidines (thymine and cytosine) approximates the number of purines (adenine and guanine). |
| 1953 | James Watson and Francis Crick derived the three-dimensional and double-helical model of the DNA |
| 1958 | Frederick Sanger discovered the first and complete protein structure - insulin. |
| 1977 | Fred Sanger sequenced the genome of a bacteriophage which contained more than 5000 nucleotides. Sequenced the DNA of the human mitochondrial |

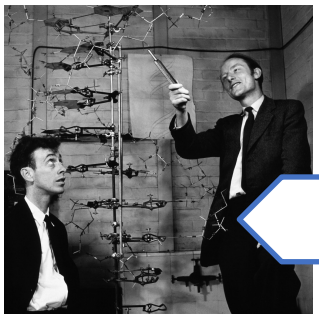

Robert Hooke, invented the microscope (1665)

**1839** German physiologist Theodor Schwann, after a lovely dinner with his mate Schleiden and a chat about nuclei, realised that animals were comprised of cells too and stated: **"All living things are composed of cells and cell products"**

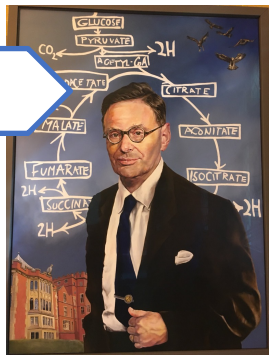
Theodor Schwann,
Cell theory (1839)



Eduard Buchner,
Cell free fermentation, and the role of the "enzyme" (1900s)



Hans Krebs,
Krebs cycle (1937)




Watson and Crick,
3D helical model of the DNA(1953)

***Lets remember them, lest they be forgotten***


# Top 10 biochemistry News of 2020 - A Round-Up

*https://www.bioexplorer.net/biochemistry-news-2020.html/*

1. Crispr gene editing awarded Nobel Prize in 2020: Emmanuelle Charpentier and Jennifer A. Doudna awarded a joint Nobel prize for CRISPR/Cas9 system discovery [Germany-USA]
2. The spike of the pandemic getting filmed: COVID19spike protein visualized and studied [UK, July 2020].
3. A new type of antiviral molecule developed [Netherlands – Switzerland, December 2020]
4. The double-edged blade of amyloid proteins turns to slay influenza – Researchers develop synthetic amyloids to battle viruses [ Belgium, June 2020].
5. Damage me, and you will die -a new type of chemicals that kill fungi discovered on damaged surfaces of plants [Switzerland, November 2020].
6. Mining sea invertebrates for medicine – a potent antifungal was found hiding inside the sea squirt [USA, 2020].
7. Tea and chocolate to the rescue: chemicals produced by popular plant products can block an essential enzyme of the SARS-CoV-2 virus [USA, November 2020].
8. Lighting up cell chemistry – scientists have found a new enzyme activated by blue light [Germany, May 2020]
9. A combination of modern methods helped establish the structure of an important enzyme that is involved in making fats [USA, March 2020].
10. Breast milk can protect young children against obesity due to a special fat molecule [USA, November 2020].

# What vitamin D does in lumbar disc disease.

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Vitamin D is essential in maintaining a healthy mineralized skeleton by regulating calcium and phosphate metabolism in vertebrates including humans. The active form of vitamin D (Vitamin D3 / cholecalciferol) is generally synthesized in human skin by a photochemical reaction driven by the ultraviolet rays of the sunlight from a steroid precursor. Vitamin D3 not only regulates the uptake of dietary calcium but also regulates the balance of bone calcium and phosphate. Further, it is associated with the musculoskeletal function in humans. Presently deficiency of vitamin D is a major health concern worldwide. In recent years, researchers have found that insufficiency and deficiency of vitamin D is associated with many chronic diseases.

Low back pain (LBP) associated with lumbar disc herniation (LDH) is a major health problem which leads to low quality of life and loss of work. In addition, increased cost for diagnosis and treatment approaches is an added burden.

Various hypotheses explain vitamin D deficiency as a contributing factor for LDH, lumbar disc herniation and degeneration (LDHD) which ultimately give rise to LBP.

The initial manifestations of vitamin D deficiency may involve weakness of muscles and cause muscular pain which also contribute to LBP. Adequate vitamin D levels aids in the proper function of free nerve endings; and deficiency of vitamin D causes hypersensitivity of neuromuscular junction and sensorial hyper-innervations in muscles causing dysfunction of the neuromuscular junction which eventually leads to chronic LBP.

Intervertebral disc (IVD) is a large avascular tissue which extensively depends on the balance between nutritional supply and excretion of waste. Imbalance between these two processes leads to disc degeneration. The role of active vitamin D metabolites in nucleus pulposus and annulus fibrosus cells of the IVD have been reported. Where vitamin D inhibits and decreases production of monocyte chemoattractant protein 1, thrombopoietin,

vascular endothelial growth factor and angiogenin by human annulus cells *in vitro*. Therefore, vitamin D affects detoxification pathways which are important in disc cell nutritional balance. Hence, deficiency of vitamin D causes imbalance of nutritional supply and waste excretion, thereby it can interrupt the detoxification pathways of the disc cells leading to degeneration which in turn causes LBP. In addition, vitamin D has immune regulatory properties which can upregulate anti-inflammatory cytokines and downregulate pro-inflammatory cytokines. Further vitamin D possesses defensive mechanisms against cell injury which is caused via free radicals, reactive oxygen species, glutathione and glutamate. Therefore, vitamin D plays a role in the pain mechanism by downregulating inflammatory cytokines that produce pain (a) directly, (b) by stimulating release of pain mediators, (c) by upregulating anti-inflammatory cytokines (d) by its role in eliminating toxic metabolites (e) by increasing the antioxidant pool, hence, it is evident that deficiency of vitamin D can trigger the LBP associated with LDH. In addition, vitamin D status affects pain sensitivity and opiate activity. It is highlighted that vitamin D has an influence on proteoglycan (PG) synthesis. It also mediates the plasma sulphate concentration. Hence, vitamin D may regulate the inorganic sulphate availability for intracellular sulphation of PG, which in turn plays an important role in IVD anabolism. In addition to immune modulatory properties of vitamin D, its receptors have been identified in skeletal muscles. It also affects sensory neurons to modulate pain.

It is believed that in LDH, herniated disc tissue induces immunogenic and immunologic properties thereby initiating the pain cascade through immune activation, infiltration and cytokine release. LDH actively amplifies inflammation by producing pro-inflammatory cytokines and pain mediators. These substances have pain receptors in intervertebral disc tissues where its expression increase in LDH like inflammatory conditions. Vitamin D affects neuropathic pain by directly suppressing inducible nitric oxide and through its immunoregulatory properties. It also affects cell population that is inflamed in disc herniation, either through suppressing neurotoxic agents or by its action on neurotrophins which in turn reduces pain in LDH.

Further, vitamin D receptor (VDR) gene polymorphism has a role in the development of lumbar disc degeneration and herniation. Several studies in different ethnicities have been reported worldwide. Association of VDR in LDH and LDHD have been extensively studied. Vitamin D is mediated by VDR, a steroid nuclear receptor which is located on chromosome 12 with 5.6 kb. It is the first reported gene associated with degenerative diseases of the disc. VDR helps regulate calcium homeostasis, bone mineralization and remodeling. Some studies have reported expression of VDR chondrocytes and it was thought to increase differentiation, proliferation and maturation of cartilage. It is evident that VDR is present in IVD cells and there is a prominent role of vitamin D active metabolites in disc cells promoting regulation of cell proliferation, matrix gene expression and specific cytokines and protein production. Several pathological conditions in IVD is associated with alterations of vitamin D homeostasis. This could be explained by the pleiotropic effect of vitamin D and its involvement in bone and disc metabolism. Although, the exact mechanism of decreased VDR function is poorly understood, literature suggest that vitamin D might play a role in sulphate concentration of PG and also determine the degree of sulphation in PG, which maintains the stability of the disc.

There are two VDR polymorphisms, *Fok I* and *Taq I*, which have been studied comprehensively in relation to disc degeneration and herniation in different ethnic groups. Vitamin D receptor gene *Fok I* polymorphism has two potential starting/initiation sites known as ATG and this site is thought to have a single nucleotide polymorphism (Cytosine; C/Thymidine; T). The allelic variants of the VDR *Fok I* polymorphism code for structurally different receptor proteins. Individuals with T polymorphism have two ATG start sites and initiate translation with mRNA at first ATG sites and results in a longer protein with 427 amino acids. Presence of *Fok I* site denoted by f whereas absence of *Fok I* site denoted by F the wild type. Individuals with F wild type have C polymorphism at the start site (ACG); hence they start translation with second ATG start site, and therefore receptor protein is short with 424 amino acids. It is found that *Fok I* of VDR gene has a risk allele f, which produces a full length VDR protein, whereas F allele of *Fok I* (short allele) produces a shorter VDR protein. However, the F allele interacts with transcription factors for VDR protein more efficiently than f allele and therefore increased function of F allele than f allele of *Fok I*.

Therefore, it is suggested that f allele individuals will produce VDR with decreased function leading to increased risk of degeneration and herniation in *Fok I* due to less stabilized disc structure.

*Taq I* is the second polymorphism of VDR gene, which is found in a non-coding region of Exon 9 of VDR. *Taq I* is a C/T variation. However, presence of *Taq I* sites does not change the amino acid sequence of VDR. However, *Taq I*, risk allele t has 30 % more potential, in the role of decaying mRNA when compared to T allele. This may eventually lead to impaired sulphation of glycosaminoglycan in PG synthesis. Therefore, presence of t allele resulted in less stabilized PG, altering the stability of the disc structure leading to disc degeneration. It was reported that homozygous for the risk allele of *Taq I* (tt genotype) showed increased risk of developing osteophytes and disc narrowing when compared to normal TT genotype and studies also indicated that t allele of *Taq I* in vitamin D receptor gene was significantly associated with degenerative disc disease. A study conducted in Sri Lanka revealed that wild type homozygous FF genotype was the most prevalent genetic variant of VDR *Fok I* polymorphisms in study population and also resulted that *Fok I* polymorphism was not associated with LDH.

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# Heat shock proteins in diabetes mellitus : Role and targeting

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Heat shock proteins (HSPs) are originally identified as 'heat inducible gene products' and among the most abundant intracellular proteins that respond to a wide variety of cellular stress conditions. They are highly conserved proteins, which are expressed at low levels under normal physiological conditions. They are markedly increased in response to cellular stresses, including elevated temperature, tissue hypoxia, exposure to reactive oxygen species and genotoxic agents, heavy metal intoxication, nutrient starvation, etc. HSPs are categorized into several families based on their molecular weight (i.e HSP100, HSP90, HSP70, HSP60, HSP40). Upregulation of HSPs is vital in heat shock response, which could manage stress conditions in cells. The increased expression of HSPs under a stress condition is generally regulated by heat shock factor 1 (HSF1). HSF1 is phosphorylated and forms homotrimers, then binds to heat shock elements (HSEs) located upstream of HSPs genes and activates the transcription of heat shock genes in response to an immediate cellular stress and to a subsequent stress. HSPs primarily function as molecular chaperons, facilitating the folding/unfolding of other cellular proteins, preventing protein aggregation, transporting of cellular proteins, etc. Although HSPs are predominantly intracellular cytoprotective machineries, they can also be exposed on the plasma membrane and released into the extracellular space, resulting in detectable levels of HSPs in the blood. HSPs inhibit apoptosis and protect against both oxidative stress and inflammation, with changes in their expression and / or intracellular or extracellular location, which ultimately lead to the pathogenesis of several diseases. Diabetes mellitus is one such example.

It is widely accepted that HSPs have additional functions in their 'protein moonlighting'. HSPs improve our understanding of the pathogenesis of diabetes and reveal exciting new therapeutic opportunities. Their role in β-cell dysfunction and insulin resistance is more pronounced. Hyperglycemia leads to decreased regulation of protective HSPs. Elevated HSP27 has been associated with the pathogenesis of diabetic neuropathy and nephropathy. In addition, diabetic retinopathy has been associated with HSP70 that is inversely related to macrovascular complications. The circulating HSP 60 levels and recognition of mitochondrial impairment play a central role in the pathogenesis of type 2 diabetes mellitus, accordingly, elevated levels of HSP 60 are found in patients with type 2 diabetes mellitus. Interestingly, serum HSP 60 levels are found to be 16 times higher compared to saliva in patients with 2 type diabetes mellitus. In contrast, there is a fivefold increase in salivary HSP 72 levels compared to serum HSP 72 levels and that there is no correlation between the concentrations of salivary and plasma HSP 72. Expression levels might reflect the distinct biological functions played by these molecular stress proteins. In fact, mentioning that HSPs can be released in the extracellular space has led to the investigation of the potential use of both HSPs and anti-HSP antibodies as serum biomarkers of complications of diabetes.

The expression of HSPs is modulated in diabetic complications with preliminary proof of functional relevance. In fact, the strength of evidence varies by the degree of complications. For example, in the diabetic kidney, there is an upregulation of HSP47 is likely to be involved in renal fibrosis, but expression of cytoprotective HSP27, HSP90, HSP70, and HSP60 is unchanged in the renal cortex. This indicates an overall insufficiency of the compensatory response of HSP to stress induced by diabetes within the kidney. Unlike in microvascular complications, most HSPs (HSP90, HSP70, HSP60) are up-regulated in macrovascular disease. Apparently, it is increasingly recognized that HSPs act in a network, therefore, abnormalities in HSP clusters in diabetes mellitus are of great relevance. Data on diabetic wounds are scarce, however, the available results indicate that insufficient HSP47 may interfere with wound repair, while HSP90-α accelerates healing. Research on HSPs in the field of diabetic complications has limitations. It is difficult to interpret changes in HSP expression in target organs, as a rise in HSP expression can suggest direct involvement of HSPs in the pathogenic process, a compensatory cytoprotective response, or even both at different stages of the disease.

There is renowned interest on the potential use of HSPs as therapeutic targets particularly in diabetes and its associated complications. Diabetes mellitus causes the accumulation of damaged proteins, oxidative stress, altered mitochondrial bioenergetics, and apoptosis. In fact, enhancing the cytoprotective machinery of HSP appears to be an ideal strategy to prevent and/or reduce the progression of complications associated with diabetes. Available data in experimental animals support this hypothesis. Moreover, the recent development in cancer research of bioactive compounds that can rise/lower HSP levels in a precise manner has opened the way to pharmacological intervention studies targeting HSPs also in others pathological conditions, including diabetes-related complications. In this regard, newly developed HSP90 inhibitors appeared promising. Apparently, the pharmacological modulation of HSPs may cause undesired effects because of the multitude of HSP functions. Therefore, the development of compounds targeting specific HSP functions would be crucial in pathological conditions that require long-term therapy, such as complications of diabetes. Tissue targeting strategies may also be valuable as pharmacological modulation of HSPs that can have opposing effects in different vascular beds of diabetes complications.

Bimoclomol is an experimental drug that induces stress proteins and has cytoprotective effects. Indeed, the drug can increase the fluidity of the membrane and extend the activity of HSF-1, thus can raise the levels of HSP70. Bimoclomol has been reported to improve wound healing, reduce tissue damage, reduce diabetes complications, and improve insulin sensitivity in animal models of diabetes. Hydroxymethylglutaryl (HMG)-CoA reductase inhibitors, carvedilol, pentoxifyllin, and lipoic acid, are also examples of drugs that target HSPs. Administration of lipoic acid to diabetic neuropathy patients is associated with normalization of the low level of HSP72 with low levels of leukocyte HSP72. In this sense, the clinical improvement in neuropathy in these patients is promising. Exercise, carvedilol, and thiazolidinediones have been reported to also increase HSPs. The mechanism of increased HSP70 levels by thiazolidinediones is correlated with the anti-inflammatory action of this drug on pancreatic β cells. Nitric oxide is a potent stimulator of HSP expression. Drugs that restore the release of nitric oxide from endothelial tissues, such as β-adrenergic blockers, angiotensin-converting enzyme inhibitors, HMG-CoA reductase inhibitors and thiazolidinediones, are related to satisfactory results in clinical trials of diabetes in relation to HSPs.

However, the administration of HSPs via oral or intravenous means is relatively impractical since HSPs are primarily intracellular molecules. It has been reported that liposomal delivery of HSP72 into renal tubular cells blocks activation of NF-kB tumor necrosis factor, therefore, this blocks ischemia-induced apoptosis. To date, a number of new drugs and drug leads that target HSPs are found to improve diabetic retinopathy, neuropathy, nephropathy, wound healing, cardiac ischemia and insulin resistance in animal models. Gene delivery agents are also interesting however, systemic gene delivery in clinical practice poses exciting challenges. HSP delivery genes can benefit patients with diabetes and are a novel hypothesis that can be tested in the laboratory and clinical setting.

Recent clinical trials have shown that some functional foods can affect serum levels of anti-HSP antibodies. Food and their active components can affect complications such as atherosclerosis, inflammation, protein glycation, and β-cell survival. Thus, each drug or food constituent that affects the HSPs can play an important role in decreasing the implications of diabetes. In conclusion, fundamental insights into how HSPs give rise to disease will be an important component of therapeutic targeting of HSPs. Potential drugs, drug candidates, and food supplements that focus on anti-HSP antibody levels targeting the treatment of diabetes and its associated complications are warranted in the near future.

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# Molecules of emotion; the new science of psycho-neurochemistry

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Emotions, previously thought to be purely psychological, have now been linked to specific chemical processors taking place through the body, and not just only to the emotional centres of the brain such as the amygdala, hippocampus and hypothalamus but other types of centres scattered throughout the body. For example, neuropeptides, playing a vital role in neural information transmission and processing, are associated with specific emotions and behaviours. Oxytocin and vasopressin having specific effects on social behaviours, maternal behaviour in the mother-child bonding process is a good example. The kind of neuropeptides available to cells constantly changes, reflecting variations in one's emotions throughout the day. The exact combination of neuropeptides released during different emotional statuses has yet to be identified.

Neuropeptides are biomolecules that regulate almost all life processors on a cellular level. They are "messenger molecules" and are involved in sending chemical messages from the brain to receptor sites on cell membranes throughout the body. An average cell has thousands of receptor sites for neuropeptides. Dr. Candace B. Pert, a molecular biologist who played a pivotal role in the discovery of the endorphin molecule, termed them as molecules of emotions.

Internal feeling state (emotions) elicits neuropeptide responses impacting even at the cellular level of the body. For example, consider a feel-good peptide such as serotonin, when it binds to its specific receptors on the cell membrane, the neuropeptide is able to transmit a feel-good message right into the nucleus of the cell. As a result, this feel-good message influences every function the cell is responsible for.

The body responds favourably to positive emotions such as joy, love, hope, optimism, kindness and humour and negatively to negative emotions such as sadness, anger, despair, loneliness, worry, and depression. Thus, it is postulated that if one is resentful, harbour anger, and sustain negative emotions, and it can have a definite negative impact on one's overall functionally even at the cellular level due to the influence of neuropeptides. What does this mean? For example, can suppressed anger or other "negative" emotions cause cancer?

Lydia Temoshok, a psycho-oncologist, has shown that cancer patients who kept emotions such as anger under the surface, remaining ignorant of their existence, had slower recovery rates than those who were more expressive [1]. David Spiegel, in 2012 has shown that being able to express emotions like anger and grief can improve survival rates in cancer patients [2].

In her groundbreaking book of *molecules of* emotions [3], Candace has attempted to formulate a theoretical model in this regard. Accordingly, emotional expression is always tied to a specific flow of peptides in the body. The chronic suppression of emotions, such as suppressed anger, disturbs the natural flow of neuropeptides.

One good example is the process of carcinogenesis. Every one of us has several tiny cancerous tumours growing in our bodies at every moment. The part of the immune system responsible for the destruction of these errant cells consists of natural killer cells whose job is to attack these tumours, destroy them, and rid the body of any cancerous growth. In most of us, most of the time, these cells do their job well, which is a job coordinated by various brain and body peptides and their receptors. Thus, these tiny tumours never grow large enough to cause us to become ill. However, in a situation where this natural flow of peptides is disrupted, the activity of the natural killer cells will be impacted. This means our emotions facilitate the flow of the peptide that direct these killer cells at any given moment. Therefore, it is all about establishing the natural flow of neuropeptides

We, humans, create "perceptions" about life situations or events. This mental habit distances us from the true nature of things. This act of judgmental thinking creates an incessant stream of thoughts, making the mind heavy, which inturn interrupts the natural flow of molecules of thoughts, neuropeptides.

There is a large body of evidence on how humans can counter the stress response by using a combination of approaches that elicit the relaxation response. These include deep abdominal breathing, focus on a soothing word (such as peace or calm), visualization of tranquil scenes, repetitive prayer, yoga, and tai chi.

The practice of Mindfulness focuses one's attention on one's thoughts, actions, and present moments nonjudgmentally has recently gained popularity over many contemplative practices as an approach to elicit and relaxation response. There is a plethora of evidence on the benefits of mindfulness practice [5,5,6], and its potential applications are yet to be explored.

Description of the technique of mindfulness practice. [7].

1. Find a quiet and comfortable place. Sit in a chair or on the floor with your head, neck, and back straight but not stiff.

2. Try to put aside all thoughts of the past and the future and stay in the present.

3. Become aware of your breathing, focusing on the sensation of air moving in and out of your body as you breathe. Feel your belly rise and fall; the air enters your nostrils and leaves your mouth. Pay attention to the way each breath changes and is different.

4. Watch every thought come and go, whether it be a worry, fear, anxiety, or hope. When thoughts come up in your mind, do not ignore or suppress them but simply note them, remain calm, and use your breathing as an anchor.

5. If you find yourself getting carried away in your thoughts, observe where your mind went off to without judging and return to your breathing. Remember not to be hard on yourself if this happens.

6. As the time comes to a close, sit for a minute or two, becoming aware of where you are. Get up gradually.

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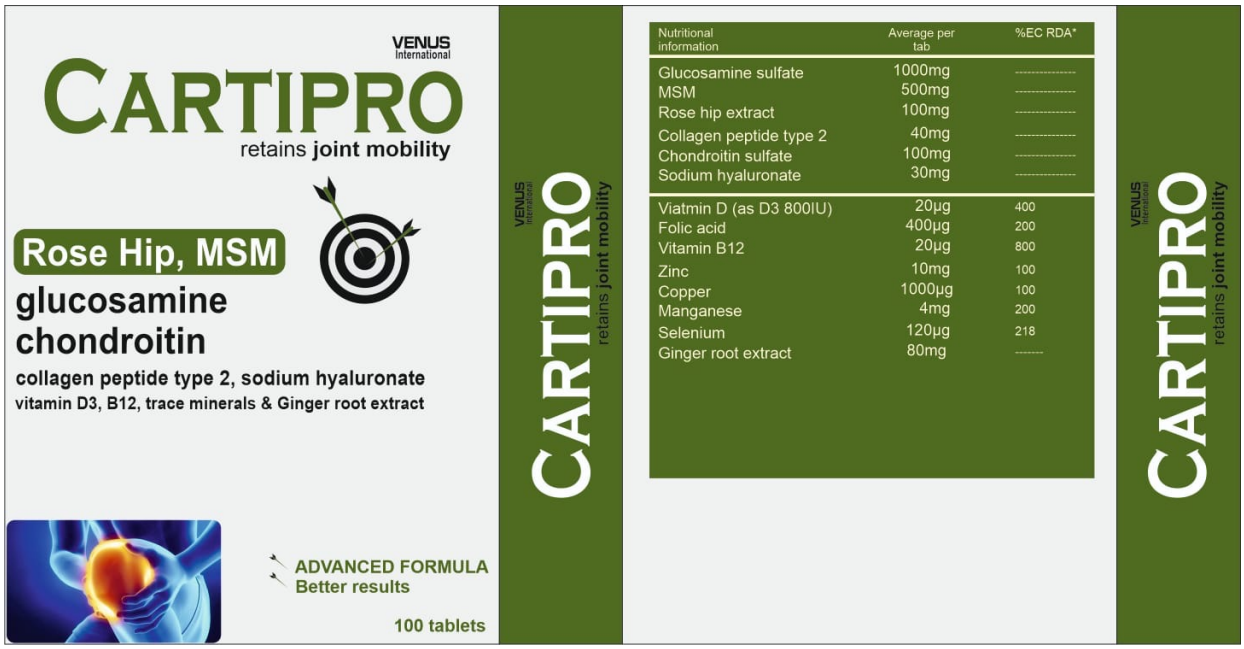



**"In Ostio & Rheumatoid Arthritis - To reduce pain, To improve tendon and joint flexibility"**

# CONNECT WITH US:

**We welcome contributions to the Newsletter from CBSL members for the following**

- ❑ Original photographs for the cover page
- ❑ Articles
- ❑ Letters to the editor
- ❑ Research highlights

**Please submit to newsletter.cbsl@gmail.com**

**Cover page photograph**

Vertical A4 size, 210 x 297mm / 4961 x 7016 pixels

**Articles**

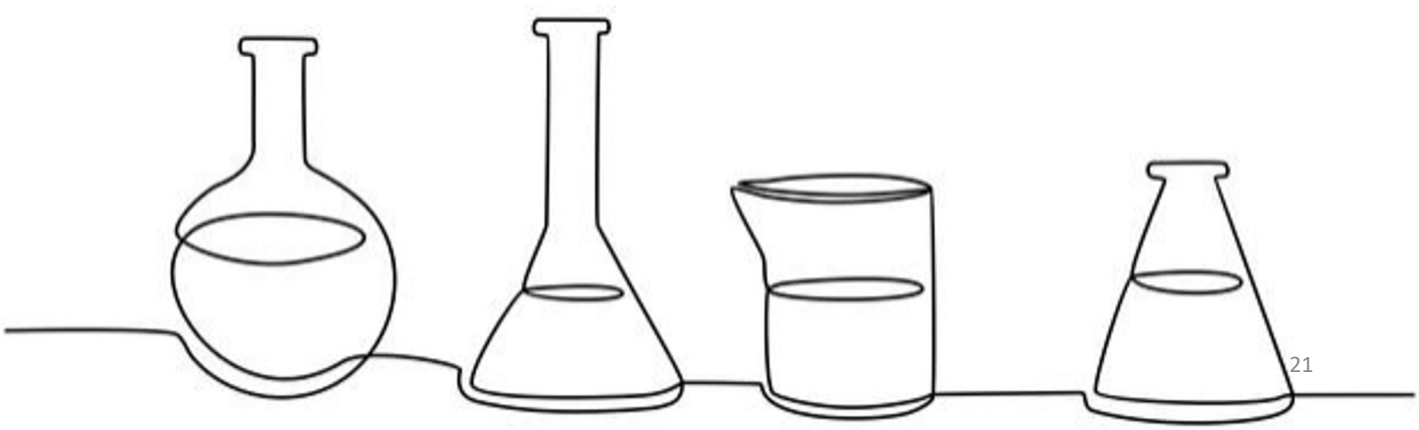
Articles should have a descriptive title, should not exceed 1500 words, including not more than 10 references, and include authors name (s), academic degree (s) and institutions(s), along with a photograph.

**Letters to the editor**

Letters should have a descriptive title, and should not exceed 500 words, including not more than 10 references. Begin with the salutation " to the Editor" and close with the authors name (s), academic degree (s) and institution (s).

**Research Highlights**

Short description on Research highlight, with a photograph



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