

Impact of *Yoga* upon the DNA repair mechanism of the body

Rishov Mukhopadhyay^{1*}, Sanjay Kundu², Monojit Debnath³ & Moulisha Biswas³

¹School of Pharmacy, University of Nottingham, Nottinghamshire-NG7 2RD, United Kingdom;

²Ajanta Pharma Ltd. Charkop, Kandivili (West), Mumbai-400067, Maharashtra, India;

³Bengal Institute of Pharmaceutical Sciences, Kalyani, Nadia-741235, West Bengal, India

E-mail: pharma.rishov26@gmail.com

Received 30 January 2017, revised 13 March 2017

Yoga is considered to be one of the oldest sciences developed as per precedence, where merging certain simple postural movements with basic physiological actions, have proved to be revitalising for both mind and body. The present study is focussed upon the basic chemistry that underlies this phenomenon. The impacts of *yoga* upon the DNA repair mechanism of the body, where we have tried to find out how *Yoga* can activate the glutathione production in the body, which is the innate antioxidant agent. Thus, helps to prevent and/ or alleviate necrotic pathophysiological conditions as well. We have also compared cases where people doing *yoga* are living a better life than people who are debarred from it, where improvement in their mental well-being as revealed Electro Encephalogram investigations.

Keywords: *Yoga*, Glutathione, Rejuvenation, Electro Encephalogram, Diseases

IPC Int. Cl.⁸: C12P 21/02, C07K 5/037, A61B 5/00, A61K 39/135, C12N 5/22, C05F, A01N 1/00, B29C, C07K, C12N, A43D, B64F

Background

Yoga has been documented to be one of the oldest therapies of non-invasive medical procedures to alleviate and prevent disease and other pathophysiological conditions of human body. Amazing combination of exploiting various bodily postures and regulation of oxygen consumption during the processes forms the basis of the age long success of this clan as a popular traditional medical technique. Origin of *yoga* dates back to around 5000 years ago somewhere on the northern areas of India contemplated by a sage Patanjali, today honoured to be the father of Modern *Yoga*. The exact time about the preaching and flourishing of this medical wonder could not be traced back since very little could have been deciphered about this sage compared to other contributors of Indian traditional medicine yet percolating through time this art of living flowed down generations and is still in prominence. The detailed documented description of Swami Jnaneshvara Bharati as “*Yoga Sutras of Patanjali*” mentioned the basic principles of the technique. He described the process as a physio-psychological approach to wellbeing including practices like

Concentration (*Dhyana/ Samadhi Pada*), where the process of introspection has been explained – ways through which one can explore one's insight can actually make us realise our mental milieu¹. A study by M. Kox *et al.* (2012) explained that during this process it activates the sympathetic nervous system along with subsequent release of catecholamines/ cortisol release attenuating the innate immune response and activating anti-stress² and anti-inflammatory responses³ besides initiating the major processes like gluconeogenesis and glycogenolysis aiding in metabolic homeostasis of the body⁴.

This review explains the impact of *yoga* upon the innate production of glutathione and their contributions towards cell rejuvenation and DNA repair mechanisms, an insight towards its applications for preventing various metabolic and necrotic disorders of the body.

Practices (Sadhana Pada): This *sutra* describes many philosophical aspects among which it also tells about *Asanas* (basic postural exercises) and *Pranayamas* (basic breathing exercises). Excluding others, our focus was to study profoundly the gross impact of these induced activities on molecular rejuvenation of human health, since in a wide array it controlled the oxygen supply to the body, where for a

*Corresponding author

considerable time the body became prone to stressful responses. Regular practise of *yoga* had been reported to shield the effect of oxidation in body⁵.

The other two practices like Progressing (*Vibhuti Pada*) and Liberation (*Kaivalya Pada*) were more having a philosophical insight directed towards psychotherapeutic aspects towards human wellbeing and were not a matter of focus for our present study^{1,5}.

The Molecular insights

Considering the basic acts involved in *Yoga*, it was found that this form of technique involves a correlated approach of psychological and physiological explorations that is not only the concern for a preventive and/or curative approach to the body but also they had considered the emotional impact of mind over physiological milieu.

Correlating the study upon improvement of glutathione status of the body with regular practise of *yoga*^{5,6} and the overall alleviation of anxiety and stress due to *yoga* gave us a basic insight towards this theoretical approach⁷⁻⁹.

Glutathione (GSH) by nature is a water soluble tripeptide found in all cells of the body, consisting of 3 amino acids in its structure: Glutamine (Glu), Cysteine (Cys) and Glycine (Gly) (Fig. 1). It has a thiol group that contributes to its potent reducing nature, making it a potent innate anti-oxidant; effective even in millimolar concentrations. It has been found to be catalysed by Glutathione-S-transferase (GST) and Glutathione Peroxidases (GPx). Coming to its interact able sites, we can observe that it has one hydrogen bond donor moieties and nine hydrogen bond acceptor moieties, where there is still a controversy regarding the intra-molecular hydrogen bonding by the sulphahydrl (-SH) group¹⁰. The carboxylate moieties on either side can also form bonds like hydrogen bonding, charge-charge interaction and charge dipole interactions¹⁰. Now, inside body, due to several endogenous and exogenous factors, oxidative stress is formed resulting in agents like ROS (Reactive Oxygen Species), RNS (Reactive Nitrogen Species), etc., which causes oxidative damage to DNA resulting in apoptosis. These species are chemically electron deficient, which contributes to their reactivity. They gather electrons from different chemical moieties specially DNA bases, making them reactive and thus hampers cellular stability resulting in necrosis and cell death^{10,11}.

Thus, to prevent such consequences, the body has an endogenous agent to be activated as a defence mechanism– Glutathione (GSH). Glutathione reduces such oxidative species in the presence of Selenium dependent GSH Peroxidase, where GSH itself is oxidised to GSSG but does not form another reactive species since immediately after then it is reconverted to GSH by GSSG Reductase at an expense of NADPH. Thus, this innate redox cycle maintains the whole equilibrium of the body, which at severe pathophysiological condition gets hampered and thus causes various necrotic and metabolic disorders including cancer¹¹.

Synthesis of GSH in body is highly influenced by the level of ATP supply from the body where regular exercises with proper supply of oxygen to the body tissues has been found to increase the ATP generation in body¹².

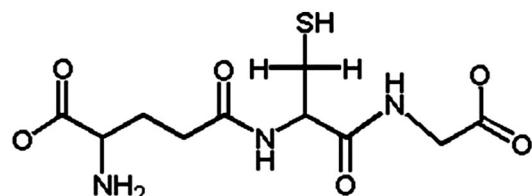
Mechanism of the antioxidant action of glutathione

Oxidation in the body can occur due to various reasons among which naturally it occurs with advancement of age. But apart from that pollution, diet, lifestyle, drug induced, pathological consequences, etc., can contribute profoundly towards this process. This results in cellular degradation in body through hampering the DNA.

Chemically oxidative damage mostly occurs at the guanine residues of DNA due to its high oxidative potential compared to the other bases. A recent study has established that the two oxidised form of guanine potentially contributes towards cellular instability as depicted alongside¹³⁻¹⁵ (Fig. 2).

The ROS, RNS, H₂O₂, etc., generated in the body, carries out this oxidation by stabilising themselves, taking up electron from the guanine base. This process occurs in a chain system and includes DNA surrounding the affected one. Thus, this oxidation continues like an epidemic and hampers the stability of all the surrounding cells as well. Thus, more necrotic cells are formed and ultimately the viscera get damaged leading to cancer.

Figs. 3-6 depict the whole process of how above mechanism occurs in the cells. Here, the endogenous glutathione plays a vital role where they replenish the electron deficiency of the oxidised DNA bases but they get reduced. Recycling of GSH is a redox reaction involving 2 vital steps- de novo synthesis and recycling of GSSG as depicted alongside in Fig. 7.¹³



GLUTATHIONE (GSH)

Fig. 1 — Structure of Glutathione (GSH)

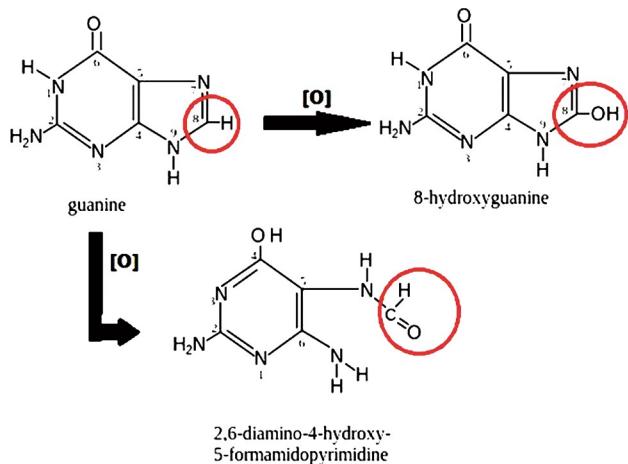


Fig. 2 — Oxidised forms of Guanine bases in DNA due to oxidative stress

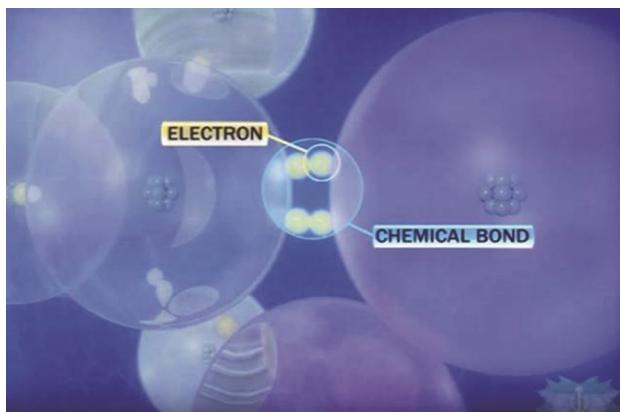


Fig. 3 — Cells having normal chemical interaction and stable milieu

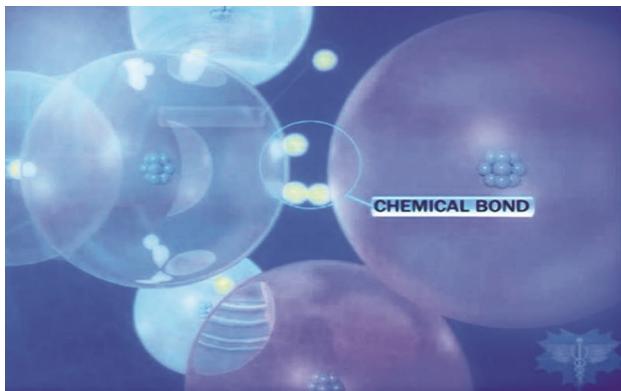


Fig. 4 — Oxidative stress causes cellular oxidation resulting in loss of electrons inducing reactivity in the moieties

Thus with proper nutrient supply to the body, if we can adequately provide oxygen supply then body will produce more ATP. Practicing *Pranayam* every day in a routine manner not only increases the capacity of our lungs but also increases the oxygen supply to the body, which positively impacts upon the production of ATP in mitochondria^{12,16}.

Discussion

The purpose of this study was to establish the relation between the physical and the physio-molecular aspects of the age old Science of *Yoga* and how practicing *Yoga* can be a non-invasive and non-medicinal option to alleviate many common and major diseases. Keeping in mind the psychological benefits, the study was further correlated. During the study it was observed that though *Yoga* apparently might include only a collection of physical exercises

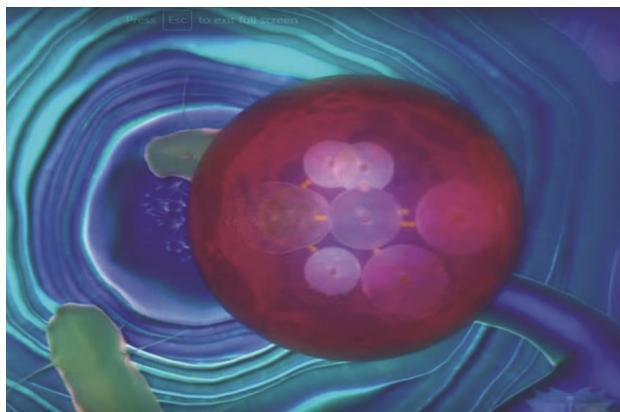


Fig. 5 — Generation of oxidative species like ROS, RNS, etc., in cells

These reduced glutathione are reconverted to Glutathione by a redox reaction as discussed earlier. Hence, the oxidative reaction meets an inhibition¹⁶.

Now, the focus of discussion would be how *Yoga* impacts upon this biochemical process? As discussed in the previous sections that one of the most important requirement for the synthesis of endogenous Glutathione is ATP, which can be generated in the body by increasing cellular and metabolic activity.

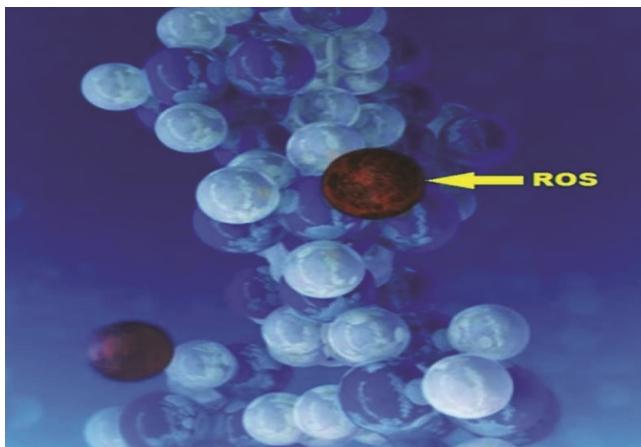


Fig. 6 — Interaction of ROS with the DNA moieties which would result in DNA damage

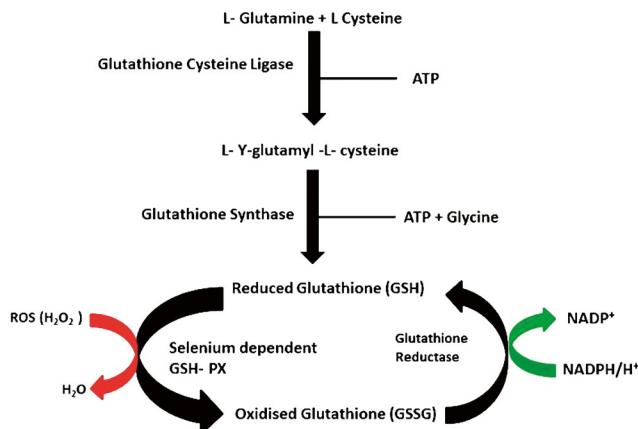


Fig. 7 — Biosynthesis and biochemical fate of Glutathione in body

but has grave impact upon the innate metabolic processes of our body, among which mainly the focus was on the DNA repair mechanism. Increased level of oxygen along with proper and balanced supply of nutrition makes one healthy, this is something which we always know as a proverb but the present study aimed to establish the scientific mechanism that underlines this concept.

Now coming to the physio-philosophical aspects of the *Yoga*- the *Asanas* and the *Padas* (*Vibhuti Pada* and *Kaivalya Pada*) includes the mental or cognitive rejuvenation of the body though inducing a positive wave inside the mind by philosophical interactions and inducing positive thoughts through spiritualism. Scientifically, this enhances our mind and contributes to our good mood. A compact study was done in reference to Hoffman (2012) and Tiffany (2010) suggested an observation on a set of 30 people

divided into 2 groups of 15 people each where one group had an exposure to *Yoga* while the other one was kept out of it. A 14-Channels Electro Encephalogram study showed increase in Alpha (α) and Theta (θ) waves in the Frontal and Parietal lobes of brain in people exposed to *yoga*. This study was further supported by another article "Alpha (α) brain waves boosts creativity and reduces depression" published in the book "The Athlete's Way" by Christopher Bergland and also posted in Psychology today website on April 7, 2015. Thus, it can be inferred that developed cognition can be an indication of neuronal stabilisation and rejuvenation. But still the question persists as to why these benefits are occurring? What bio-chemical mechanism is underlying the phenomenon? As per recent established literatures, dose dependent presence of glutathione in the neurones and astrocytes prevented the cells from dopamine induced damage. Now, this infers to the preventive and curative aspect of *Yoga* against diseases like Parkinsonism and other neurodegenerative disease, since in previously mentioned studies we can find out how *Yoga* influences enhanced production of glutathione in the body. Also, other necrotic diseases including cancers can be prevented by regular practise of *yoga* besides being saved from common respiratory troubles, since it includes a profound exercise of the respiratory system through *Pranayams*¹⁶.

For metabolic disorders including non-insulin dependent Diabetes mellitus it has been observed that the deleterious effects of hyperglycemia by incurring over deposition of ROS in the pancreatic β - cells, leading to impaired production of insulin. Also, in certain recent researches, it has been mentioned how *Yoga* induces the metabolic consumption of glucose in the body, which prevents over deposition of glucose in blood. Moreover, by initiating glycogenolysis, it induces breakdown of deposited fat in the body, hence helps in cholesterol chipping and prevents formation of plaques in blood vessels, which might be otherwise would have caused atherosclerotic symptoms^{4,17}.

Conclusion

Concluding the study I would like to infer the mystical effects of this age old practice, which if formulated and contemplated using modern advancements, can be a non-invasive boon to prevent and cure many unanswered questions about human health. By simple mechanism of altering the oxygen supply to the body along with certain scientifically

developed body movements can alleviate and even cure various metabolic diseases, where modern medical science is still on an arguable scaffold.

History beholds many other precedence of the preventive and curative aspect of this age old art where a famous *sloka* prevalent among *Yoga* practitioners mentions in Sanskrit about the vast advantage of *yoga* and their prayer to The Founder of *Yoga*, Patanjali:

Yogena Cittasya Padena Vaacaam |
 Malam Shariirasya Ca Vaidyakena ||
 Yo[a-A]paakaro[a-U]ttamam Pravaram Muniinaam |
 Patan.jalim Praan.jalir-Aanato[a-A]smi ||

Meaning

- 1 - (I bow down to him who purifies the impurities of the mind (by removing the *Chitta Vrittis*) by *Yoga*, who purifies the expression of speech by *Pada* (Grammar),
- 2 - and (who purifies the) impurities of the body through *Vaidya* (Medical Science),
- 3 - He who is an expert in removing the impurities of the body, mind and speech, to that most excellent of *Munis*,
- 4 - (Who is) Patanjali, I bow down with folded hands.

Acknowledgement

Author would like to acknowledge my co-authors and my friends both in India and The United Kingdom for their constant support in this endeavour, which I believe is the driving force for any contemplation to be an innovation some day.

References

- 1 Bharati SJ, *Yoga Sutras of Patanjali-Interpretive Translation*, (Online resource: Swami Jnaneshvara Bharati), 2011, 22-59.
- 2 Kox M, Stoffels M, Smeekens SP, van Alfen N, Gomes M, *et al.*, The Influence of Concentration/Meditation on Autonomic Nervous System Activity and the Innate Immune Response: A Case Study, *Psychosomatic Med*, 74 (2012) 489-494.
- 3 Coutinho AE & Chapman KE, The anti-inflammatory and immunosuppressive effects of glucocorticoids, recent developments and mechanistic insights, *Mole Cell Endocrinol*, 335(1) (2011) 2–13.
- 4 Christiansen JJ, Djurhuus CB, Gravholt CH, Iversen P, Christiansen JS, *et al.*, Effects of Cortisol on Carbohydrate, Lipid, and Protein Metabolism: Studies of Acute Cortisol Withdrawal in Adrenocortical Failure, *The J Clin Endocrinol Metab*, 92 (9) (2007) 3553–3559.
- 5 Ross A & Thomas S, The health benefits of yoga and exercise- A review of the comparison studies, *J Altern Comple Med*, 16 (1) (2010) 3-12.
- 6 Michalsen A Grossman P, Acil A, Langhorst J, Lüdtke R, *et.al.* , Rapid stress reduction and anxiolysis among distressed women as a consequence of a three-month intensive yoga program, *Med Sci Monitor*, 11 (2005) 555–561.
- 7 Li W, The effects of yoga on anxiety and stress, *Altern Med Rev*, 17 (1) (2012) 21-35.
- 8 Dillard CJ Litov RE, Savin WM, Dumelin EE & Tappel AL, Effects of exercise, vitamin E, and ozone on pulmonary function 7 and lipid peroxidation, *J Appl Physiol*, 45 (1978) 927–932.
- 9 Evelo CTA, Palmen NGM, Artur Y & Janssen GME, Changes in blood glutathione concentrations and in erythrocyte glutathione reductase and glutathione S-transferase activity after running training and after participation in contests, *European J Appl Physiol*, 64 (1992) 354–358.
- 10 Rosei MA, Hydrogen bonding by the sulphydryl group of glutathione, *M A Experientia*, 35 (1979) 1178.
- 11 Friedman M, In: *The Chemistry and Biochemistry of the sulphydryl group in amino acids, peptides and proteins*, (Pergamon, Oxford), 1973, 21-73.
- 12 Wibom R, Hultman E, Johansson M, Matherei K, Constantin-Teodosiu D, *et al.*, Adaptation of mitochondrial ATP production in human skeletal muscle to endurance training and detraining, *The Am Physiol Soc*, 73 (5) (1992), 10.
- 13 Guilford FT & Hope J, Deficient Glutathione in the Pathophysiology of Mycotoxin-Related Illness, *Toxins*, 6 (2014) 608-623.
- 14 Ballatori N, Krance SM, Notenboom S, Shi S, Tieu K, *et al.*, Glutathione dysregulation and the etiology and progression of human diseases, *The J Biol Chem*, 390 (2009) 191–214.
- 15 Anderson ME, Glutathione: an overview of biosynthesis and modulation, *Chemico- Biol Interact*, 111 (2) (1998) 1–14.
- 16 Brigelius FR, Tissue-specific functions of individual glutathione peroxidases, *Free Rad Biol Med*, 27 (1999) 951–65.
- 17 Yang H, Amber ML, Prabha S, Pattharee P, Linda E, *et al.*, Neurochemical and Neuroanatomical Plasticity Following Memory Training and Yoga Interventions in Older Adults with Mild Cognitive Impairment, *Frontiers Ageing Neurosci*, 8 (2016) 277.