



REVIEW ARTICLE

INTEGRATED APPROACH OF YOGA THERAPY (IAYT) HAS AN ABILITY TO TREAT CANCER PATIENTS: A REPORT BASED ON ELECTROPHYSIOLOGICAL MECHANISMS

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INTRODUCTION

Cancer is one of the most feared diseases, a leading cause of death worldwide, considering for nearly 10 million deaths in 2020 and most common were breast, lung, colon & rectum, prostate, skin, cervical & stomach. In 2022, as many as 14,61,427 cancer cases were registered compared to 14,26,447 in 2021 in India. The corresponding figure for 2020 was 13,92,179," the data showed. Among states, Uttar Pradesh topped with 2.10 lakh new cases – up from 2.01 lakh in 2020. Around one-third of deaths from cancer are due to tobacco use, high body mass index, alcohol consumption, low fruit and vegetable intake and lack of physical activity. Adverse effects of its treatment (chemotherapy, radiation & surgery) and diagnostic procedures (biopsies & radiological diagnostic scans) can cause financial, physical, psychological, and emotional problems affecting patients' quality of life.

Despite the availability of powerful technology, strong and targeted medicines the desired therapeutic success in cancer care remains an elusive goal for the modern medicine. Cancer survivors will continue to increase or will not be affected, will have long peaceful life, if IAYT or complementary and alternative medicine (CAM) is taken as an important part in life. Not much financial burden is there to accept this as an important & essential tool in our life. About 38% persons in USA are using CAM for managing pain, arthritis, cardiovascular diseases, cancer, emotional problems like stress, anxiety, depression. Yoga, the mind-body medicine of CAM, is comprised of a wide range of techniques, which gradually harmonizes the body and mind as compiled by Patanjali in his yoga sutras. Yoga has been used by Hindus and Buddhists for thousands of years for maintaining good health as well as spiritual practice. Yoga is now practiced worldwide by millions of people irrespective of their age, gender, race, religion, and nationality.

The main purpose of this review is to familiarize cancer patients and their caregivers (oncologists, nurses, family members and patients) with the research evidence of the beneficial effects of yoga and to encourage more scientifically focused research so that yoga therapy (IAYT) is fully recognized and integrated into cancer therapeutic programs. Life depends on continuous input of energy because living cells require continuous assembly, maintenance, and selective destruction (turnover) of complex structures. These include both molecular (RNA, DNA, and proteins, etc.) and physical structures (membranes, organelles, etc.), as well as maintenance of non-equilibrium distributions of small molecules and ions(1-6). Energy input is needed to overcome both the negative entropy associated with making and maintaining order and the positive free energy associated with synthesis of the many required molecules. Providing and maintaining a robust, stable source of energy for doing chemical and physical work is the first and most essential requirement for the existence of life. Step-1 to 5 shall be important to understand the role of IAYT on treating cancer individuals and description of positive aspect of IAYT is based on electrophysiological mechanisms. Some risk factors (Step-1) are mentioned which can affect both parasympathetic and sympathetic nervous system. Metabolic homeostasis (Step-3) if fully maintained (adequate) through mitochondria with the presence of oxygen to parasympathetic stimulation (Step-2). If delivery of oxygen is less, mitochondrial injury occurs, metabolic homeostasis would be poor. Ionic environment in the cell remains normal with parasympathetic and opposite with sympathetic (Step-4). Exchange of ions across the cell membrane (Electrophysiological processes) gets normal and more powerful with parasympathetic but not with sympathetic. Mitochondrial injury leads to inflammation, concentration of ROS increases, mutation in the cell takes place and even cell can be multiplied uncontrolled ways which leads to cancer(Step-5) but with proper ionic concentration both inside and outside the cell will lead to powerful healthy life in the individual.

What is IAYT?: Integrated Approach of Yoga Therapy (IAYT) is an individualized, personalized, and holistic approach that considers patient’s mind, body, and spirit. This practice helps to diffuse anxiety and sadness, harmonizing system for the body, mind, and spirit. Physical exercises, the physical components of yoga practices (only Asanas) and integrated approach to yoga therapy have several similarities, but also have important differences. Evidence suggests that IAYT appear to be superior to both physical exercise & yoga practices in most outcome measures. Emphasis on healthy life nourishing diet, a healthy and natural environment, a holistic lifestyle, adequate bodywork through Asanas, mudras and Kriyas, invigorating breath work through the use of pranayama and the production of a healthy thought process through the higher practices of Jnana and Raja yoga might be a more scientific and useful than only yoga (breath regulation, mindfulness during practice, and importance given to maintenance of postures) or physical exercise. The IAYT model is based on *Pancha Kosa* concept; various yogic practices are incorporated at each level to help subjects as therapeutic interventions with different disorders deal with their problems. IAYT bring the central nervous system (CNS), autonomic nervous system (ANS) into healthy balance by stimulating the parasympathetic nervous system (Figure-1). When our body & mind are threatened or perceives being stressed (+ve or -ve stress), sympathetic nervous system is stimulated (Figure-2), blood sugar level is gone up (Hyperglycaemia). In contrast, opposite responses are observed when subject is at rest/relaxation or no stress (Figure-2)

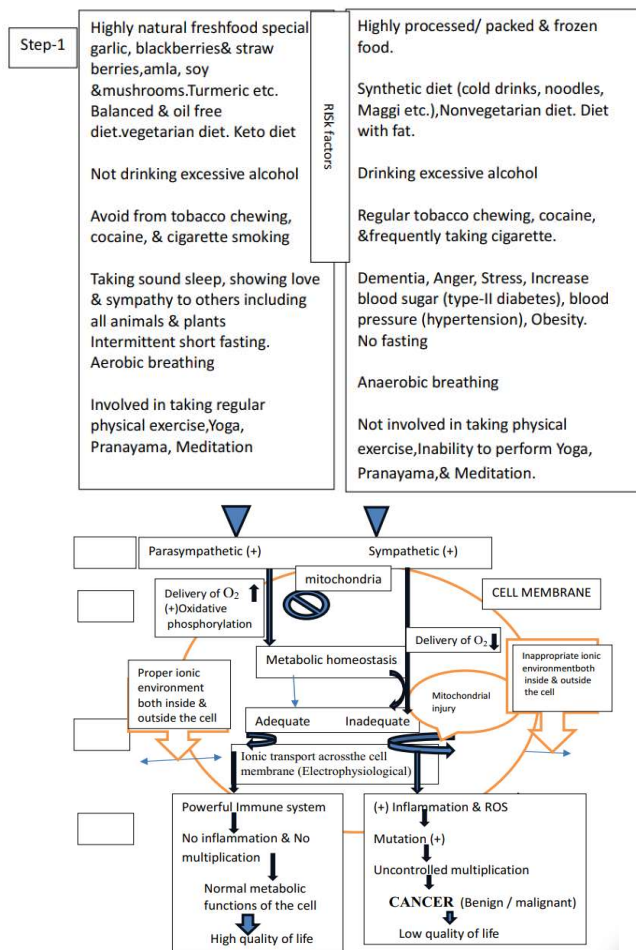


Figure 1, Step-1-5, A flow chart showing characteristics of a cell to various risk factors

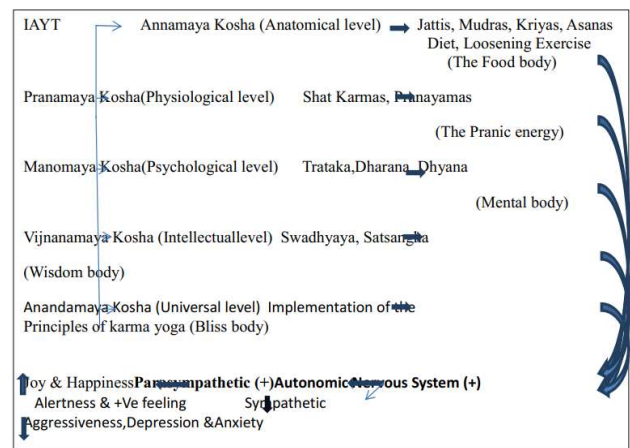


Figure 2. Implementation of IAYT based on Pancha kosha where involvement/stimulation of autonomic nervous system (ANS) especially parasympathetic nervous system (PNS).

Basic regulatory pathways in IAYT: Formal meditation practice can change both brain structure & function (7). Continuous practice can increase thickness of prefrontal cortex (PFC), amygdala, insular cortex (INSULA) & left hippocampus which have an active role in long term memory formation, emotional regulation & cognition (7). This is done through stimulating autonomic nervous system (ANS). Regular Surya namaskar, yoga also can bring awareness & joy by stimulating parasympathetic nervous system (figure 2). ANS, both sympathetic (SNS) & parasympathetic (PNS) can act on endothelial cell (EC), vascular smooth muscle cell (VSMC), nodal & contractile cell in heart (Figure-3). Metabolic activity in these cells starts from binding with either adrenergic or cholinergic receptors. There may be a contraction & relaxation depends upon metabolic activity in the cells. Arterial compliance depends upon availability of gas transmitters (H₂S, CO, & NO) which regulate the metabolic activities in these cells resulting vasoconstriction or vasodilation (9-10). As a result, myocardial contractility, heart rate (HR), respiratory rate (RR) are altered and accordingly changes on blood pressure is also notified (Figure-3). Several important alterations are noted while following ‘Pancha kosha’ (7). These are (1) Stimulation of muscle spindle & Golgитendon organ (receptor for balance and tone), (2) Stimulation of vasomotor centre, (3) Stimulation of central nervous system (CNS). All these together can involve autonomic nervous systems (PNS or SNS) (Figure-3).

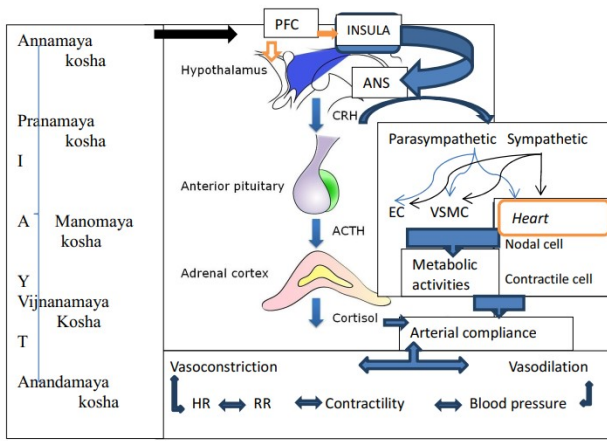


Figure 3. Possible neuroendocrine pathways involved in IAYT

Endothelial cells (EC), Vascular smooth muscle cell (VSMC), nodal & contractile cell in heart are come into operation and the finale output depends upon either sympathetic (SNC) or parasympathetic (PNC) (Figure-3). Hypothalamic-pituitary –adrenal (HPA) axis is also affected due to stimulation of limbic system (amygdala, hippocampus), Vascular responses depends on the secretion of corticotrophin- releasing factor (CRF),which act on pituitary for adrenocorticotrophic hormone (ACTH) which subsequently stimulates the adrenal cortex for cortisol (7). Effect of cortisol includes increase blood sugar level leading to deterioration of balance between collagen and elastin- a main and important component for arterial compliance(12). In case of parasympathetic stimulation, less or no cortisol, hence vasodilation and blood pressure come down (Figure-3).

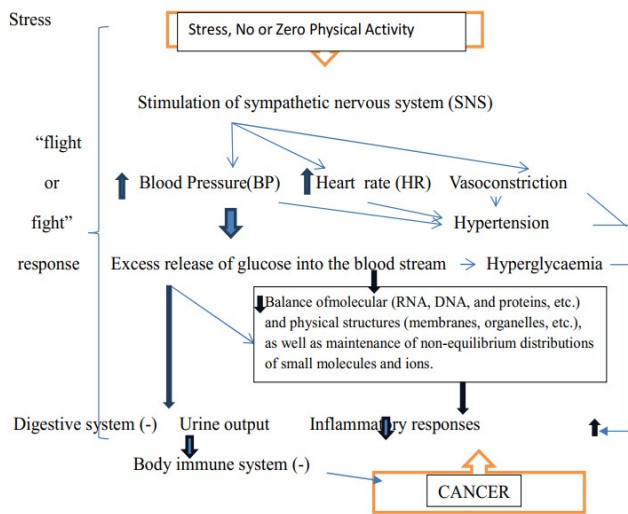


Figure 4. Response of sympathetic nervous system to stress/zero physical activity

Basic functions of autonomic nervous system in IAYT: a) **Sympathetic (flight or fight response):** Stress is part of our lives. Responses of stress includes 1) Stimulation of sympathetic nervous system which can increase blood pressure, heart rate, respiratory rate, 2) Blood glucose concentration in increased due to more secretion of cortisol which can increase blood glucose level, even more increase leads to hyperglycaemia,3) Body immune system is inhibited due to hyperglycaemia. Graphical representation (Figure-4) is given below. Subject has a chance to develop both hypertension and hyperglycaemia. These responses (flight & fight response) can be corrected after following IAYT (7).

Parasympathetic (rest& digest response): The parasympathetic nervous system is stimulated when one relaxes (Figure-5). Blood flow to the digestive system, brain, extremities & sexual organs is

increased. metabolic activity in vascular tissues is adjusted, resulting blood pressure (BP), heart rate (HR) & respiratory rate are reduced or becomes normal (signs of improved parasympathetic tone). No sign and symptoms of both hypertension & hyperglycaemia (7). Subjects with all age groups feel joy, happiness, can decrease negative feeling of aggressiveness, depression, and anxiety (7). Yoga practices can increase multiple neurotransmitters and hormones such as GABA, serotonin & dopamine-all natural anti- depressants (7). These neurotransmitters and hormones can increase the level of melatonin, helping to initiate sleep, improving sleep quality and also can help to secrete more oxytocin, the “bonding hormone”, thus helping with feeling of connectedness (Figure-5)(7).

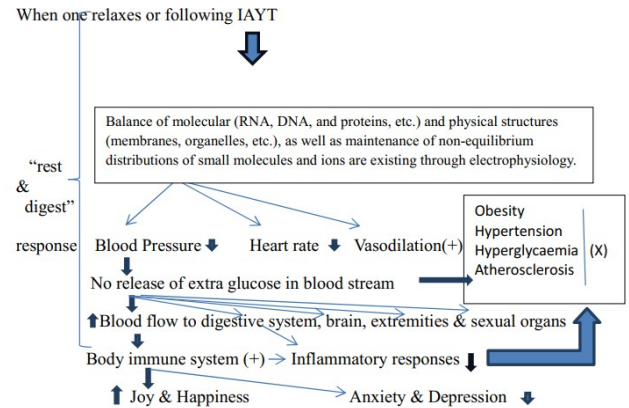


Figure 5. Response of parasympathetic nervous system to a state of relaxation/IAYT

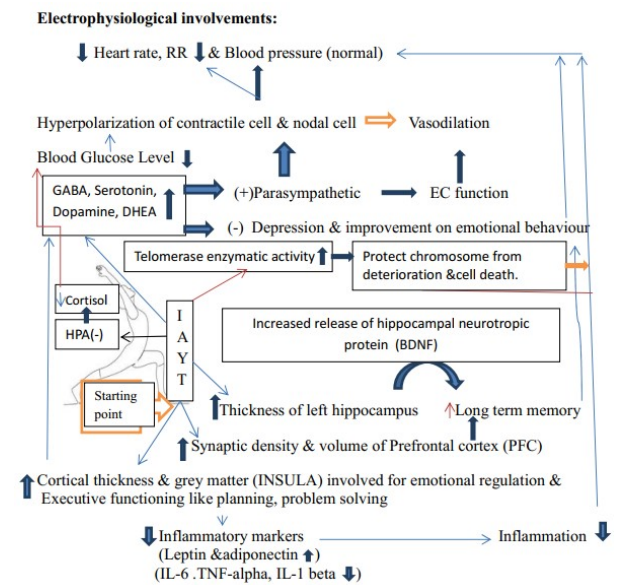


Figure 6. Co-relation between the function of autonomic and various vascular cells to following IAYT

Co-relation between the function of autonomic and various vascular cells following IAYT: Endothelial dysfunction and autonomic nervous system dysfunction are both risk factors for cancer. There is a close interrelationship between these two systems. In hypertension, endothelial dysfunction affects the pathologic process through autonomic nervous pathways, and the pathophysiological process of autonomic neuropathy in diabetes mellitus is closely related with vascular function (11-14). However, detailed mechanisms of this interrelationship have not been clearly explained. In this review, we summarize findings concerning the interrelationship between vascular function and the autonomic nervous system may provide more comprehensive risk stratification and a new effective therapeutic strategy against atherosclerosis, hypertension and hyperglycaemia leading to cancer (7,11-14). Following important findings are noted. 1) Endothelial cell (EC) function is affected against ANS. Endothelial cells, vascular smooth muscle cells & nodal cells get hyperpolarized

when there is a stimulation of PNS, resulting heart rate decreases, blood pressure goes normal, respiratory rate is also reduced.2) HPA axis is inhibited, less cortisol can reduce blood sugar level, hyperpolarization process in these vascular tissues will be operated, resulting normal arterial compliance. 3) More release of GABA, serotonin, dopamine, dehydroepiandrosterone (DHEA) can control emotion &behaviour (7, 11-19).4) Less secretion of inflammatory markers would reduce inflammation. 5) Vascular function is nicely maintained, means process of contraction and relaxation of vascular smooth muscle, cardiac muscle would be proper with parasympathetic dominance (Figure-6).6) Telomerase enzymatic activity is increased which can protect cell deterioration and cell death (Figure-6) (7).Synaptic density and volume of prefrontal cortex left hippocampus which can increase the long-term memory through increased release of neurotropic protein (BDNE). 8) Concentration of inflammatory markers is decreased, resulting no inflammation which again will help in maintaining blood pressure, atherosclerosis, and hyperglycaemia (7).

Basic molecular controlling mechanism of sympathetic (SNS) and parasympathetic (PNS)in vascular system: Resting Membrane Potential (RMP) in nodal fibre (pacemaker fibre) is -60 mv &-90 mv in contractile fibre in the heart (Figure-7). With the help of “funny Na⁺ channel”, ‘T’ type Ca⁺⁺ channel and ‘L’ type Ca⁺⁺ channel, K⁺ channel, electrical event goes on rhythmically, making nodal cell & contractile cell active till death. Some additional voltage gated Na⁺ channels are also operated in contractile cell to make resting membrane potential -90 mv during resting condition. Neurotransmitters like acetylcholine (Ach) or adrenaline/noradrenaline (Epi / NE) play an active role during the process of depolarization, repolarization and hyperpolarization expect only one plateau phase in contractile fibre present in heart. Hence, neuroendocrine process to IAYT cannot be overruled.

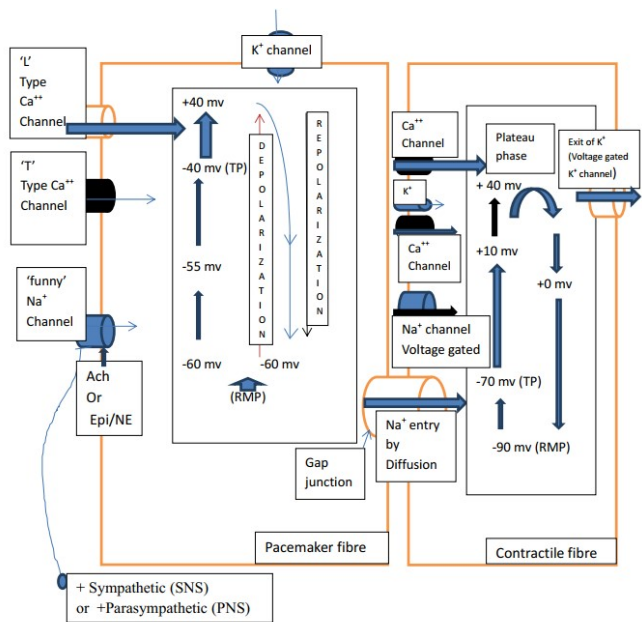


Figure-7. Basic mechanism of sympathetic and parasympathetic in vascular system

Responses from general basic extrinsic innervation of vascular system: -a) Sympathetic Nervous System (SNS)- In this, stimulatory G protein(GS) after binding with adrenergic neurotransmitter (Epi/NE) in the membrane can convert GTP to GDP as soon as adrenergic receptors are stimulated. GDP can form cAMP from ATP which stimulate protein kinase A. Protein kinase has a big role to stimulate voltage gated Ca⁺⁺ channel, quick depolarization takes place. Cardiac output, stroke volume and heart rate are increased which can increase blood pressure (Figure-8).

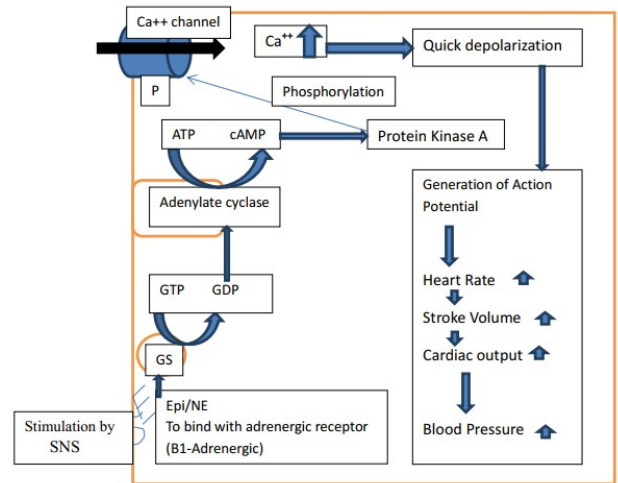


Figure 8. General basic extrinsic innervation of vascular system (Sympathetic response)

Responses from general basic extrinsic innervation of parasympathetic only on nodal cell (pacemaker fibre): Parasympathetic (vagal) activation, which releases acetylcholine onto the SA node that binds to muscarinic receptors having three units (α, β & γ), decreases pacemaker rate by increasing potassium conductance and decreasing the pacemaker currents. Cyclic adenosine monophosphate (cAMP) is less produced due to stimulation of alpha unit of muscarinic M2 receptor (Figure-9). These changes in ion currents decrease the slope of phase 4 of the action potential, thereby increasing the time required to reach threshold. Voltage gated potassium channel is directly inhibited by β and γ unit of muscarinic receptor (Figure-9).

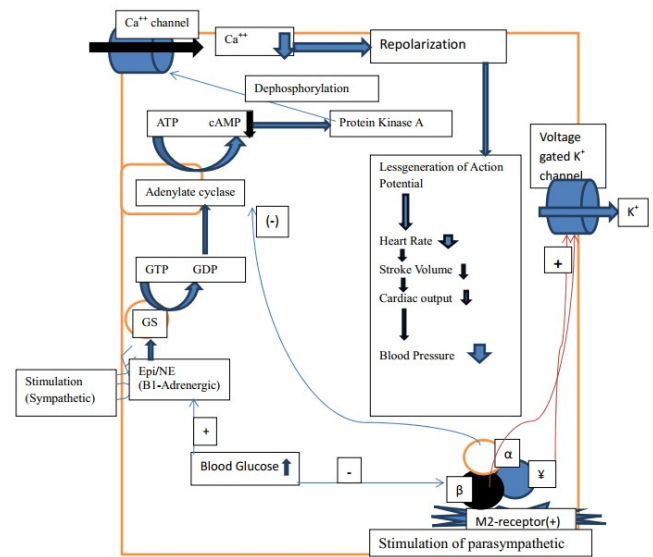


Figure 9. General basic extrinsic innervation of parasympathetic only on nodal cell (pacemaker fibre)

Vagal activity also hyperpolarizes the pacemaker cell during Phase 4, which contributes to the longer time to reach threshold voltage. Heart rate & blood pressure are reduced.

DISCUSSION

Sympathetic on contractile is stimulatory. Following IAYT, few important changes are noted. 1) Concentration of gaso transmitters (NO, CO, H2S) is increased (15-17), resulting inhibition of ryanodine receptors which reduce the transport of Ca⁺⁺ from sarcoplasmic reticulum to cytosol, hence formation of Ca⁺⁺ - calmodulin complexes.

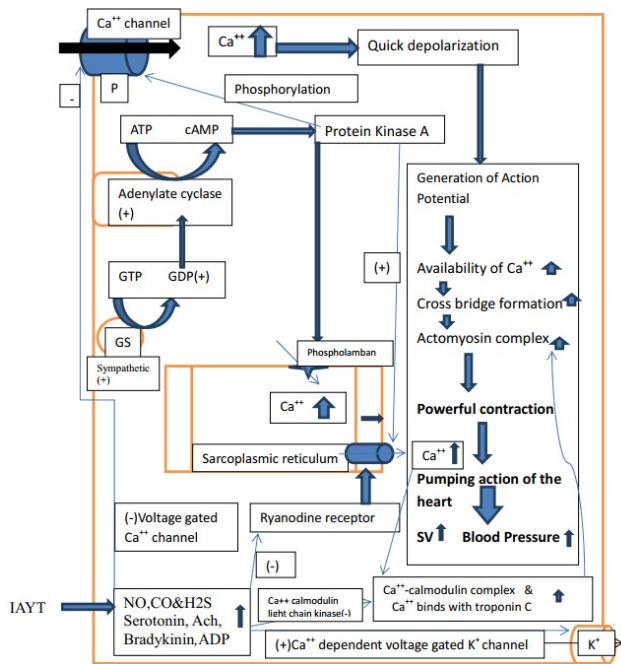


Figure 10. Response of sympathetic on contractile cell & possible mechanism to IAYT

Less amount of formation of cross bridges takes place. Concentration of Ca⁺⁺ in the contractile fiber decreases, but concentration in the sarcoplasmic reticulum is increased. 2) Concentration of serotonin, acetylcholine, bradykinin, and ADP are increased, have inhibitory effect of ryanodine receptor, has an inhibitory effect on Ca⁺⁺-calmodulin light chain kinase, resulting formation of less amount of Ca⁺⁺-calmodulin complex. 3) Gasotransmitter along with serotonin, bradykinin and ADP has a stimulatory effect of Ca⁺⁺ dependent voltage gated K⁺ channel, and hence this is again inhibitory, allow fibre to relax (Figure-10).

Conclusion (Diagrammatic):

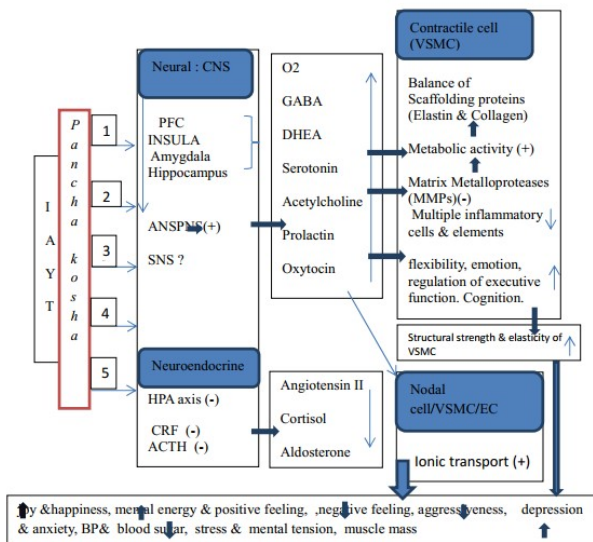


Figure 11. Schematic representation on role of IAYT on cancer treatment based on electrophysiological mechanisms

CONCLUSION

Electrophysiological mechanism is being operated in every cell in our body and which has been regulated by nervous system and endocrine system. Regulation will decide the responses of a cell. World Health Organization (WHO) estimates that 80% of non-communicable diseases (NCD) deaths are due to four main disease types: cardiovascular disease, cancer, diabetes, and respiratory diseases.

Unfortunately, lifestyle is the major causative factor on NCDs, including tobacco use, sedentary lifestyle, and lack of regular exercise, unhealthy diets, and chronic psychological stress. Chronic inflammation and stress are a common factor of many of the NCDs, and an area where IAYT has been found to be extremely beneficial. IAYT can reduce stress with increased *parasympathetic* and reduced sympathetic activities respectively. Yoga practices (IAYT) can help to lower blood pressure, increase lung capacity, improve respiratory function, and heart rate, improve circulation and boost muscle tone.

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