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# Universal Dietary Adjunct Therapy

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**Abstract:** *HEALTH can alternatively be also said as most synergistic aging to chronological age. Thus, figuring out approaches that lay path to reducing age, or simply anti-aging approach, help in this synergy, may even bypass this age constraint to some extent. In year 2009, a large scale European cohort study “MARK AGE STUDY” was designed to understand the aging changes aimed at reducing aging process or if possible stop it. Although there were many finding in the study, one in particular the oxidative changes associated to aging process, showed lower lycopene and MDA levels; and higher cysteine,  $\alpha$ -tocopherol and 3-nitrotyrosine levels in long living individuals<sup>1</sup>. However, following failure to find any dietary indication or supplementation, in relation to this study, it was sought possible to come with a dietary indication that would benefit in reducing the aging process. In year 2020, COVID 19 has emerged as a pandemic, which shows age related severity. So certain principles are created, and first applied in COVID 19 context, and evidences in favour of it were examined. A dietary instruction has been formulated labelled as Universal Dietary Adjunct Therapy, and is recommended to be included in normal dietary habits for a longer life-span, and as prophylaxis for chronic diseases and as adjunctive therapy to terminal illness and no-cure scenarios.*

**Keywords:** *covid19, mark-age project, health, anti-aging diet, diet, universal adjunctive diet therapy, UDAT.*

## I. INTRODUCTION

COVID19's majority of cases cure on its own, with mild to no distress. So, a “threshold”, may be multifactorial, if crossed, could avoid mortality, or reduce severity. Increasing immunity is the general approach, but just a body function, which can be improved further if health is improved<sup>2,3</sup>. A peak human system would be one that doesn't require an outside environment but rather its own system to survive, like an ecosystem. It can be interpreted to be said as, “the net changes a body could undergo would be net zero (ex: healing its damages while recovering 100% functionality), would be an ideal. A more realistic approach would be attaining best physiological state, with exogenous attenuation of possible negative changes. Best physiological state without exterior intervention should be healthy aging, i.e. most synergistic aging to chronological age, and exogenous attenuation of possible negative changes will be redox changes body exhibits. The closest description of such is in regard to MARK-AGE project. The intention is to attain the most synergistic aging to a human capacity. Mathematically, (biological age  $\approx$  chronological age); or, (biological age < chronological age), if possible.

In COVID 19, decreased mortality and morbidity among younger individuals is seen. So why not make every one young, or simply approach it. MARK AGE project large scale consortium, with one of the objectives to create a diet and a clinical regimen,<sup>4</sup> here is a dietary intervention. MARK AGE STUDY<sup>4</sup> and multiple small scale studies<sup>5-8</sup> provide info as to how aging is effecting normal human functioning.

## II. METHOD

With no existing protocol for anti-oxidant requirements, it has been postulated and estimated in multiple papers. Here, ageing, and redox biomarker, association has been interpreted initially independently, and a theory been hypothesised. Then its proof or evidence has been collected through, randomly searched databases on Google scholar using random analogously thought keywords, without any bar on publication year with intent of finding factors that alter aforementioned biomarkers, and antioxidants levels. However for specific redox markers and antioxidants, recent systematic review papers on PubMed have been selected. The goal is to achieve biological aging as in genetically superior long living families, and it was seen it could be possible to mimic those findings of specific redox markers through a dietary approach, and some fundamentals of such diet has been created.

## III. BIOMARKERS OF AGEING

Mark age project concluded, antioxidant lycopene was lower in older population, as well as, in offspring of longer living individuals (GO), and their spouses (SGO). GO and SGO also had higher levels of cysteine and  $\alpha$ -tocopherol. And among redox biomarkers, lower malondialdehyde and higher 3-nitrotyrosine levels were seen.<sup>1</sup> These biomarkers in light of anti-ageing diet have been explained with their principles and dietary utility.

### A. Lycopene

It is a major carotenoid in human plasma, and tissue, not classified as an essential nutrient; is taken mostly from diet, and dietary absorption decreasing with age.<sup>9</sup> Also, carotenoid uptake in older individuals shows significant health improvement. A dietary modification to decrease in its consumption and reaching lower levels is obvious, but aforementioned facts contradict each other. It would only make sense if increased utility of lycopene is based on behavioural/dietary activity in GO and SGO, which may saturate the lycopene utility pathway, lowering plasma levels. It shows high tolerance and lower toxicity, and has an antioxidant function, showed in different researches. It doesn't have any recommended daily dose.<sup>9,10</sup> Increase in plasma levels after a five day meal,<sup>9</sup> and increased antioxidant activity, when taken with olive oil, but not when consumed alone.<sup>10,11</sup> Effect of lycopene supplementation on two biomarkers of lipid peroxidation, namely LDL oxidizability, and urinary F2-isoprostanes, shows no effect.<sup>12</sup> The beneficial effect of tomato with olive oil,<sup>11</sup> show existence of dietary factors with may help in saturating lycopene utility pathway. Also Medium doses of oral lycopene supplements, and not the higher doses, where found to be more effective, thus limiting factor/s are involved. Multiple papers indicate interaction of lycopene with other active compounds is crucial for obtaining optimum function in human health, and some beneficial actions maybe a function of its isomers or metabolites.<sup>9-12</sup> Thus, Higher uptake of the lycopene is the first step. And secondary consumption of dietary complementing factors. Interaction of lycopene with active compounds is crucial for obtaining optimum function in human health, and some beneficial actions maybe a function of its isomers or metabolites.<sup>9-12</sup> Lycopene is found in Tomato,<sup>11</sup> papaya,<sup>13</sup> carrot, watermelon<sup>14</sup> etc. It has poor bioavailability, and poorer in old age,<sup>9</sup> so probiotics is help in absorption. Lycopene is heat sensitive, and simultaneously show trans to cis isomerisation and cis-isomer is highly bioavailable.<sup>15</sup> Papaya raw fruit show 2-9 times higher bioavailability than raw carrot and tomatoes.<sup>13</sup> Watermelon juice increase lycopene levels in postmenopausal women 3 fold.<sup>14</sup> Dosage: High dose lycopene for 5 days, once or twice a month, along with vitamin C rich food thrice daily 8 hours apart,<sup>16</sup> during high dose lycopene period followed by low dose lycopene every day. Lycopene up to 100 mg/day hasn't shown side effect, in clinical studies. In animal studies even 200 mg/kg didn't show any side effects either.<sup>9</sup> Lycopene toxicity causes lycopenaemia, i.e. reddish discoloration of body which retracted soon after the dietary change and didn't show any significant symptoms.<sup>17</sup> Caution: Lycopene, being heat labile, is mostly embedded in food matrix. Use heat to break down food matrix and avoiding heat mediated lycopene degradation, to increase bioavailability.<sup>10</sup> Few instances of lycopene based diet have been studied and used here framework for expected dietary intervention.

- 1) Tomato-onion-olive oil puree heated for 2 hours (showed z-isomerisation which is highly bioavailable).<sup>15</sup>
- 2) Watermelon consumption, twice per week,<sup>14</sup>
- 3) chop tomatoes into 16 small pieces, and heat with olive oil, for at least 10 mins, cis isomerisation increases with heating, at 1 hour it shows highest cis form (>90%), so a choice is dependent on users<sup>11</sup>
- 4) Air dried tomatoes>sun dried tomatoes<sup>10</sup>
- 5) raw papaya fruit consumption, one serving each day per week, than and later alternate days.<sup>13</sup>

### B. 3-Nitro tyrosine (3NT)

Increased only in GO, and not SGO, thus a genetic adaptation. It is a product of tyrosine nitration, mediated by peroxynitrite dependent, peroxynitrite independent, and free radical mediated pathways. Thus, an increased serum level is either more tyrosine nitration, via any tyrosine nitration pathway; or decreased 3-nitro tyrosine catabolism. The major contribution is by peroxynitrite alone. In entire mechanism of 3NT, including action, formation and elimination, only tyrosine radical formation is associated with multiple essential benefits.<sup>1,18</sup> Dietary elements changing 3NT levels in favour of process has been postulated:

- 1) *Peroxyntirite dependent*
  - a) N acetyl cysteine decreases peroxyntirite formation.<sup>19</sup>
  - b) Herbs: Choi et al, showed peroxyntirite scavenging potency of different herbs; Witch hazel bark, rosemary, jasmine tea, sage, slippery elm, black walnut leaf, Queen Anne's lace, and Linden flower. Choi et al, also found Hamamelitannin, as major active component of witch hazel bark with strong peroxyntirite scavenging.<sup>20</sup>
  - c) Vitamin C: water soluble, highly bioavailable, give extracellular protection against peroxyntirite.<sup>21</sup> Citrus family fruits like kiwi, mango, and vegetables such as broccoli, tomatoes, and peppers.<sup>22</sup>
  - d) Quercetin: lipid soluble, show intracellular protection against peroxyntirite.<sup>21</sup> Found in red onion, grapes, blueberries, cherries, apples and broccoli.<sup>5</sup> Its bioavailability can be increased by a) with vitamin C, non-digestible fibres, or breaking the food matrix. Taking up with dietary fat can helps in absorption.<sup>23</sup>
  - e) (-)-epigallocatechin gallate: best known inhibitor of peroxyntirite meditated tyrosine nitration.<sup>24</sup> Found in green tea, cocoa.<sup>5,25</sup>

## 2) Protection Against Peroxynitrite Independent Enzymatic Peroxide Action

- a) Glutathione endogenous production is increased by NAC,  $\alpha$ -lipoic acid, raw liver, whey protein, or milk thistle.<sup>26-28</sup>
- b) Selenium: Brazilian nuts, eggs, and chicken are major sources. However, caution should be taken against selenium toxicity and deficiency.<sup>29</sup>

## 3) Free radical scavengers for decreasing free radical/heavy metal transitional state mediated 3NT formation.<sup>18</sup>

Vitamin C, at high intravenous doses, shows rapid recovery in critically ill covid 19 patient,<sup>30</sup> and may be beneficial in Covid 19 infection.<sup>3</sup> Quercetin, has shown to reduce virus host interaction of covid 19 with ACE-2, and has been identified with senolytic properties, and was found to be potentially affective against COVID19 disease.<sup>8</sup> Meals have been suggested based on available research materials:

### a) For Peroxynitrite Mediated

- Vitamin C with Quercetin:
  - i) Vitamin C: 5-9 servings of fresh citrus fruits or animal sources like animal liver.<sup>22</sup>
  - ii) Quercetin is lipophilic, so together would be good for extracellular and intracellular scavenging, respectively<sup>21,23</sup>. Breakdown food matrix or decrease its size as much as you can, maybe using a shredder, and increase in use of quercetin rich food in regular meals. Use oil to incorporate, or simply incorporate it into meals.<sup>23</sup>
- (-)-epigallocatechin gallate:
  - i) 2-3 cups of green tea a day prepared by brewing at 100 °C for 9.50 min with water/tea concentration 70.0 mL/g, and 230  $\mu$ m gives highest antioxidant property<sup>31</sup>. So try to approach as close as possible;
  - ii) consume cocoa (raw dark chocolates).<sup>5</sup>
  - iii) N acetyl cysteine: discussed below

### b) Peroxide Scavengers

- Glutathione: NAC is preferred, but spike in glutathione levels is followed by rapid decline, so regular uptake in small dosages throughout day.<sup>32</sup>
- Selenium : Brazilian nuts, fish, eggs, fortified food consumption.<sup>29</sup>

## C. Cysteine

a semi essential amino acid, whose supplementary form, NAC show decreased peroxynitrite production in alveolar macrophages of lung pathologies.<sup>19</sup> A therapeutic intervention of NAC has been described for covid 19 disease.<sup>33</sup> It also boosts glutathione levels, which is involved in endogenous antioxidant system, exhibiting anti-aging properties,<sup>28</sup> documented for use against covid.<sup>32,34,35</sup> Selenium is needed for optimal glutathione activity.<sup>26,29</sup> Selenium is effective in COVID.<sup>3</sup> Vitamin B complex deficiency is harmful for Covid 19 patients.<sup>3</sup> Vitamin B6, B9, and B12 deficiency impairs cysteine metabolism, and they together with Vitamin C in attenuation of methionine toxicity. Methionine toxicity show death on 10 fold consumption and morbidity at 5 fold.<sup>36</sup> Cysteine is found in animal and cereal proteins (beef, egg, whole grains).<sup>37</sup> Cysteine levels is increased by methionine consumption.<sup>32,34</sup>

Dosage: a) very small amounts of food items rich in methionine throughout day<sup>32,34</sup>, and food items containing vitamin B6, B9, and B12 levels once daily;<sup>36</sup> b) Cysteine rich food in low dosage in each meal. Higher cysteine levels cause cysteine kidney stones, prevented by maintaining urine alkalization and good hydration through citrus juice and mineral water respectively.<sup>38</sup> Regular consumption of Cysteine may cause inhibition of in vivo cysteine synthesis.

## D. $\alpha$ TOCOPHEROL (Supplementary Form of Vitamin E)

A well-known antioxidant, and used as dietary supplement, and therapeutic administration. It is increased in GO and SGO.  $\alpha$ -tocopherol supplementation lowers dietary bioavailability of vitamin E, and  $\alpha$ -tocopherol, and  $\gamma$ -tocopherol levels are responsible for antioxidant and prooxidant action respectively,<sup>39</sup> indicating composition of food sources while consuming vitamin E rich food should be considered. Second, vitamin E is a group of compounds, comprising of tocopherols and tocotrienols. The supplementary form of vitamin E is  $\alpha$ -tocopherol which shows toxicity at higher doses (>1000mg/day), but this toxicity is not observed with dietary vitamin E uptake. Further, tocotrienols show biological activities not shown by tocopherols. Synthetic and organic tocotrienols are structurally different and human receptors show seterospecificity, while there is no in vivo isomerisation of these compounds. Thus, dietary form of Vitamin E is superior to supplementary form of vitamin E.<sup>40,41</sup> An increased uptake of Vitamin E rich dietary sources, rich in  $\alpha$ -tocopherol, and tocotrienols, and low in  $\gamma$ -tocopherol is recommended.

Vitamin E supplementation has no protective effect, and has been postulated as may be harmful in covid 19.<sup>3</sup> But the mixed reports of benefits and harm, whether alpha tocopherol or vitamin E as a whole, is in favour of use of dietary form of vitamin E. Don't take tablets of  $\alpha$ -tocopherol. Avoid food sources rich in  $\gamma$ -tocopherol and  $\delta$ -tocopherol.<sup>39</sup>

### E. Malondialdehyde

A biomarker of lipid peroxidation, and oxidative stress, is a reactive electrophile species; forming covalent protein adducts, Advanced Lipoxidation End products (ALE), Advanced Glycation end products (AGE) and several types of mutagenic DNA adducts. High MDA level is seen in high fatty foods consumption, and rancid food uptake; and low MDA level in high fruit and vegetables consumption.<sup>42</sup> Our approaches to lower its level are 1.) Decreasing MDA synthesis would imply lowering lipid peroxidation, and it would refer to free radical scavengers, and reactive species scavengers, both ROS and RNS.<sup>26,42,43</sup> 2.) Increasing MDA excretion, being water soluble,<sup>42</sup> increasing body water turnover. 3.) Decreasing MDA action can be done by taurine,<sup>44</sup> NAC, carnosine,<sup>43</sup> histamine,<sup>45</sup> and melatonin<sup>43,46</sup>. Among them, carnosine is better than NAC.<sup>43</sup> Apart from dietary sources, regular exercise of moderate to severe intensity,<sup>42</sup> and pharmacological administration of folate supplementation and vitamin D3 supplementation has shown to decrease levels of malondialdehyde.<sup>17,27,47-49</sup> No direct link between vitamin D and covid 19 severity was accounted.<sup>50</sup> Taurine shows cytoprotective effect via induction of mitochondrial biogenesis, restoration of mitochondrial membrane potential, and partly restoration of NO generation.<sup>44,51</sup> Taurine reduce oxidative stress in diabetes,<sup>52</sup> and in protective in lung pathologies.<sup>53,54</sup> Carnosine protect against cross linking by non-enzymatic Glycation, is helpful in neurodegenerative diseases, like Alzheimer, which is also age-related disease.<sup>43,51</sup> Melatonin helps maintain circadian rhythm, removes unsaturated carbonyls and protect against oxidative stress.<sup>46,55</sup> Histamine makes stable products with MDA,<sup>45</sup> but is associated with allergic reactions and food poisoning, so excluded. An account of carnosine<sup>2,7,56</sup>, and melatonin,<sup>57,58</sup> action against COVID 19 has been presented, to some extent.<sup>59</sup>

#### 1) Decrease MDA Synthesis

- a) *Decrease lipid Peroxidation:* via free radical, RNS and ROS scavengers like Vitamin C (guava, kiwi, strawberry orange, tomato), Vitamin E, Carotenoids (carrot, spinach), other antioxidants like lycopene, quercetin etc.
- b) *Vitamin D Supplementation:* Fish, eggs, fortified food products.<sup>27,48,49</sup>

2) *Increase MDA Excretion:* As MDA is water soluble, it can be easily excreted if some supra-hydration is maintained. Simply drinking a litre more water than everyday could do the trick.

#### 3) Decrease MDA Action

- a) Carnosine is found in chicken breasts, beef (only in animal food sources, not found in plant food sources). It is water soluble, boiling decrease carnosine level as released in water. Grilling or roasting is not advised as it increases MDA levels. Microwave heating is recommended; otherwise stewing is the second best option, as the carnosine released in water can still be consumed.<sup>60</sup> Dosage: 8.66 mg/kg body weight per day (estimated). A detailed account of dosage is available for different conditions.<sup>43,51</sup>
- b) Taurine is found in animal food products.<sup>52</sup> Increased cysteine consumption increases taurine levels.<sup>28,52</sup> It is water soluble, and on oral consumption it peaks at 1-1.5 hours after oral administration, and is excreted via bile conjugation, has renal clearance, and return to normal levels in 6 hours. Food intake delays absorption.<sup>28,52,60</sup> Boiling decreases taurine level in food, as it is released in water. Microwave heating is recommended; otherwise cooking by boiling is the second best option, as taurine released in water can still be consumed as gravy.<sup>60</sup> Dosage: 1.07 mg/kg body weight per day (Estimated). A detailed account of dosage for different conditions is available.<sup>44,51</sup>
- c) Melatonin found in pistachios, mushroom, aged/frozen berries, nuts, fruits, vegetables etc.<sup>6</sup> Tryptophan rich food products increase melatonin levels.<sup>6</sup> It has poor oral bioavailability, and is higher in female than male.<sup>6</sup> Few studied instances of melatonin diet has been mentioned in dietary form below
  - Pistachios
    - ½ to 1 serving, close to bed time with 2-3 pieces at close interval of 8-10 hours in day time.<sup>6</sup>
    - 44gm (1 serving) of pistachios in afternoon.<sup>61</sup>
  - Mushrooms, or fruits should be added in breakfast and dinner for life, or at least in two meals per day 12 hours apart.<sup>6,61</sup>
    - *Dose:* 0.2 e 5 mg for adults close to bed time. Dosage can be regulated by diet through subjective symptomatic assessment.<sup>46,55</sup>
    - *Caution:* Higher levels of melatonin induce sleepiness, so should be taken in moderate amount in night time, 1-2 hours before bed.<sup>55</sup>
- d) Cysteine (discussed above)

4) *Behavioural Approaches Affecting MDA*

- a) High fruits and vegetable consumption.<sup>42,62</sup>
- b) Exercising on a regular basis, at medium to severe intensity lowers MDA levels.<sup>42</sup>
- c) Eat food hot: Oral administration of MDA has deleterious effect, so avoiding rancid food which has higher MDA levels is a good and simple approach to maintain lower MDA levels.
- d) Smoking cessation, as smoking individuals have higher MDA levels.<sup>42,63</sup>
- e) Refrigerated animal meats show higher MDA levels.<sup>60</sup>
- f) Boiling and then grilling shows highest increase in MDA levels. MDA is present in higher amount in animal food products, but major attenuating factors taurine, carnosine, histamine, and melatonin, are also present in higher amount in animal food products. Thus, presenting a cuisine, which keeps MDA low, and its attenuating factors high in animal food products is a question of testing permutations and combinations of different meals. From currently available data, cooking by boiling to make gravy for consumption is the best available cuisine.<sup>60</sup>

	BIOMARKERS/ ANTIOXIDANTS	PRINCIPAL		APPROACH	FOOD SOURCES
1	LYCOPENE	Increasing lycopene levels along with supplements		Lycopene rich food sources	Watermelon <sup>14</sup> , Tomato <sup>12,16</sup> carrot, papaya <sup>13</sup> ,
..	..	..		Supplements which help lycopene metabolism	Vitamin C <sup>16</sup> quercetin, Vitamin E <sup>10</sup>
2.	3- nitro tyrosine	Peroxynitrite dependent <sup>18</sup>	Decrease Peroxynitrite formation	N acetyl cysteine (cysteine) <sup>19</sup>	Animal and cereal proteins (beef, eggs, whole grains) <sup>34,37</sup>
..	..	..	Protect against peroxynitrite	Quercetin	Elder berries, blueberries, cherries, onions, apples, and broccoli <sup>5</sup>
..	..	..	..	vitamin C	guava, kiwi, strawberry orange, tomato <sup>22</sup>
..	..	..	..	EPCG	Green tea <sup>5</sup>
..	..	Peroxynitrite independent <sup>18</sup>	Free radical scavenging	Free radical scavengers	Vitamin C (guava, kiwi, strawberry orange, tomato) Vitamin E, Carotenoids (carrot, spinach), other antioxidants
..	..	..	Protection against peroxynitrite independent enzymatic peroxide action	Glutathione	NAC, VIT C, VIT B, selenium rich food sources <sup>33</sup> .
..	..	..	..	Selenium <sup>29</sup>	Brazilian nut, spinach, egg
..	..	Free radical / heavy metal transitional state mediated <sup>18</sup>	Free radical scavenging	Free radical scavenger	Vitamin C (guava, kiwi, strawberry orange, tomato) Vitamin E, Carotenoids (carrot, spinach), other antioxidants
3.	Cysteine	Increase cysteine levels		Increase methionine consumption with vitamin B6, B12, B9 and C <sup>34,36</sup>	Methionine rich food sources (poultry, eggs etc.), VIT B6, VIT B9, VIT B12, VIT C(all taken together)
..	..	..		Increase cysteine dietary sources	Animal and cereal proteins (beef, egg, whole grains) <sup>37</sup>
4.	α TOCOPHEROL	Increase vitamin E levels		Increase dietary consumption of high α	Olive oil, sunflower seeds <sup>39</sup>

			tocopherol and low $\gamma$ tocopherol.	
5.	Malondialdehyde	Decrease MDA synthesis	Decrease lipid peroxidation, via free radical, RNS and ROS scavengers <sup>27</sup>	Vitamin C (guava, kiwi, strawberry orange, tomato) Vitamin E, Carotenoids (carrot, spinach), other antioxidants <sup>27</sup> .
..	..	..	Vitamin D <sup>49</sup>	Fish, eggs, fortified food products
..	..	Increase MDA excretion	Increasing water consumption	Drink water, one litre more than you do, or maintain hydration.
..	..	Decrease MDA action	Carnosine <sup>43</sup>	Chicken breasts <sup>51</sup>
..	..	..	Melatonin	Pistachios, mushroom, nuts, fruits and vegetables <sup>6</sup> , milk <sup>46</sup>
..	..	..	NAC	Poultry, egg, whole grains, sunflower seeds <sup>28</sup>
..	..	..	Taurine <sup>44</sup>	Meat, fish, dairy products. <sup>51</sup>
..	..	..	..	Cysteine rich food products- Animal and cereal proteins (beef, eggs, whole grains) <sup>34,37</sup>
..	..	Behavioural approaches	Decreased MDA plasma levels	High fruit and vegetable content in diet <sup>62</sup> .
..	..	..	..	Regular exercise of medium/severe intensity <sup>42</sup>
..	..	..	..	Avoiding rancid food (eat food hot, or refrigerate)
..	..	..	..	smoking cessation <sup>42</sup>
6.	Resveratrol	Avoid uncontrolled reactions	Avoid alteration in metabolic pathways	Red wine, grapes <sup>5</sup>

Table i Summary

#### F. A Hypothetical Challenge

Navigation through above mentioned biomarkers, may stress individual cells under less oxidative damage and decreased residual cellular garbage (DNA adducts, AGEs, ALEPs etc.). In such cellular instance, cells can approach to their individual full potential, and it may increase vulnerability to hypersensitivity reactions, or diet toxicity induced metabolic alterations, as seen in methionine toxicity.<sup>5,36</sup> To maintain and avoid such challenge, naturally occurring phytochemical especially Resveratrol is useful,<sup>5</sup> and is a part of UDAT. Curcumin also exert similar effect but appears less effective than resveratrol.<sup>5</sup> Resveratrol is found in red wine, grapes, apple, peanut, soy, berries<sup>64</sup>. It has extremely low bioavailability,<sup>64</sup> and is impossible to eat enough to reach therapeutic concentration.<sup>65</sup> However, resveratrol and its derivatives being different in potency, and hydrophobic nature of resveratrol, allows normal doses for longer durations to elicit benefits.<sup>65</sup> Few recommendations based on research are given:

- 1) Single serving of grapes, preferably after meal (dinner to be specific).<sup>65</sup>
- 2) Single serving of red wine.<sup>64</sup>
- 3) Apple, peanuts, soy or others in amount as desired. Drug interaction should be cautioned for resveratrol.<sup>5</sup>

#### IV. DISCUSSION

The basis of this deduced diet is MARK AGE PROJECT.<sup>1,4</sup> These redox biomarkers show interaction among itself. Here, lycopene may show interaction by repairing vitamin E radical, and product of this reaction can be repaired by vitamin C,<sup>10,16</sup> under following reactions:-

- 1) Lycopene + TOH<sup>+</sup> → TOH + Lycopene<sup>+</sup>
- 2) Lycopene<sup>+</sup> + ASCH<sub>2</sub> → Lycopene + ASCH<sup>+</sup> + H<sup>+</sup>
- 3) Lycopene<sup>+</sup> + ASCH<sup>+</sup> → Lycopene + ASCH<sup>-</sup> + H<sup>+</sup> <sup>10,16</sup>

	3-Nitrotyrosine	Malondialdehyde
Lycopene	↓↓(free radical scavenging)	↓↓ (free radical scavenging)
Cysteine	↓↓↓ (peroxynitrite mediated)	↓ (via BCL <sub>2</sub> )
α-tocopherol	↓ (Indirectly via lycopene)	↓ (Indirectly via lycopene + free radical scavenging)

Table iii: INTERACTION BETWEEN REDOX MARKERS OF MARK AGE PROJECT

Further, lower 3NT level can be achieved by cysteine<sup>19</sup>, tocopherol, and lycopene (free radical scavenging activity of lycopene) consumption. Higher level is in GO only, so introducing this approach is interesting as genetically superiority can be overcome to handle the outcomes of higher 3-NT. Sustaining lower MDA level is most important in GO biomarkers mimicry, and priority is lowering MDA levels first, and then lowering 3-NT. On examining evidence against COVID 19, each of these mentioned dietary mechanisms, has some extent of benefit. And so a simple blood type effect achievable by diet can be used to decrease biological age, increase lifespan, reduce age and rate of ageing as risk factor, which has enormous health benefits on non-communicable diseases. Diet recommended individually and together, should cover every disease condition where morbidity can be quantified in terms of oxidative stress, especially in advanced stages of diseases. This spectrum is broad, fitting multiple pathologies as expected. It should be applied to chronic diseases, terminal diseases, and no-cure scenarios.

## V. CONCLUSION

Cuisines can elevate anti-aging properties of diet, and such a dietary plan has been presented. The principles applied are more important than the diet or cuisine indicated. There is variation of food products in different areas, it is recommended to understand the principles and seek help of a health professional in crafting area wise economical diet. Universal Dietary Adjunct Therapy (UDAT) is dietary method when combined with existing norms of micronutrients and macronutrients will have an enormous health impact. From Mark-Age Project,<sup>1,4</sup> here is a reference to formulated diet, UDAT which will decrease the severity of covid infection in each individual; maybe even avoid the mortality, getting past the “threshold”. Here approaching synchronisation with ageing, and maybe avoiding or delaying the age expected deterioration, have the upper hand in achieving a better health. Deductions are unethical in medical science. But, the reasons for holding clinical trial are important to understand pharmacology. However, these food products are present in community for quite a long time. And their side effects are known, and well understood, and have much higher margins of safety levels clinically proven.<sup>3,6,41,51,65,66,11,12,22,23,29,31,36,40</sup>

## VI. FUTURE PROSPECT

A clinical trial to formulate the ideal dosage, and also confirm the extent to which it will be beneficial is needed. Although, combining this approach with the existing medical practice against COVID19 infection will provide a better treatment, but till what extent. Few steps in above mentioned approach, like higher 3-NT level, needs be understood, as tyrosine radical formation is beneficial for biological functions, but the cost is oxidative damage. A detailed account will be needed to evaluate, and formulate precise methods of attenuation. Oxidative stress is an on-going process, and simply managing is slower. It can be further made faster, as we should consider cellular clearing mechanisms of residuals like Advanced Glycation End Products, Advanced Lipoxidation End Products and other outcomes of reactive species like, Reactive Carbonyl Species, Reactive Oxygen Species, Reactive Nitrogen Species etc.

## VII. ACKNOWLEDGEMENT

This research did not receive any funding.

### A. Conflict Of Interest

There is no conflict of interest.

### B. Abbreviations

- 1) GO: GEHA offspring
- 2) SGO: Spouses of GO
- 3) 3NT: 3-Nitrotyrosine
- 4) GSH: Glutathione



- 5) *MDA*: Malondialdehyde
- 6) *NAC*: N-acetyl cysteine
- 7) *COVID19*: Coronavirus disease
- 8) *UDAT*: Universal Dietary Adjunct Therapy.

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