MITOCHONDRIA IN CHINESE MEDICINE
Part 2: Antioxidants

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Antioxidants have been a hot topic in nutrition and herbal medicine since observational studies in the 1980s and '90s linked the consumption of foods rich in vitamins A, C and E with lower cancer risk (Willett & MacMahon, 1984; Stähelin et al., 1991), age related macular degeneration (Seddon et al., 1994) and atherosclerosis (Steinbrecher et al., 1984). Industry quickly capitalised on this, promoting antioxidant rich "superfoods" and supplements by implying they could prevent these diseases (Cobos & Diaz, 2023). Subsequent research challenged these initial findings, but the marketing persuaded many, and still does today. This article will examine the nature of free radicals, the role they play in health and disease, how antioxidants work, how we measure them, and the problems associated with their use. In the second part, oxidative stress and antioxidant therapies in Chinese medicine will be explored through a comparison of classical theories that parallel redox biology, followed by a survey of major antioxidant rich herbs and some guidelines for their prescription.

Reactive Oxygen Species

The term oxidation derives from the observation that substances frequently react with oxygen. It had long been known that metals corrode and oils turn rancid when exposed to the air but in 1778 Lavoisier realised this was due to oxygen combining with the substance and named it oxidation, while the substance that donated its oxygen was described as reduced (Olsen, 2025). Since these occur together, the combined reaction became known as a "redox reaction."

Unfortunately, Lavoisier was not entirely correct and what is really happening is the exchange of electrons, for which oxygen has a particular affinity. Oxygen easily receives electrons from other substances, so an oxidised substance is actually losing an electron and a reduced one is gaining an electron. Despite this apparent contradiction, the traditional terms remain. One resolution is to understand that electrons are negatively charged, and so by gaining an electron, its charge becomes more negative and is reduced.

Electrons like to exist in pairs, each having an opposing spin, which makes the molecule stable. When an odd, unpaired electron is present, it becomes a radical (IUPAC, 2025) that seeks to restore balance by reacting with other substances. In living systems these radicals can react with lipid membranes, genetic material and proteins, damaging cellular structures and affecting their function.

In biology, the majority of these reactions involve oxygen containing molecules, known collectively as Reactive Oxygen Species (ROS). Oxygen is required to receive the electrons and protons that are used in the electron transport chain (ETC) for the generation of chemical energy in the form of ATP. By adding two electrons and two protons to oxygen, this process produces water (H_2O), but an estimated 0.2-2% of electrons leak from the ETC and bind to oxygen resulting in the formation of the oxygen radical, superoxide (O_2^-) (Zhao et al., 2019). This starts a chain of reactions that can damage cellular components. The Free Radical theory of Ageing (Harman, 1956) proposed that the cumulative oxidative damage to cells over our lifetime leads to the gradual degeneration seen with age and its associated diseases.

From this, it would seem advisable to eliminate ROS but recent research has revealed that ROS are used by biological systems in a number of beneficial ways (Checa & Aran, 2020), including:

1. Our immune system attacks invading pathogens with a “respiratory burst.” Once a pathogen is engulfed by a phagocyte, enzymes trigger a deliberate over-production of ROS to induce oxidative damage to the pathogen. This also acts as a signal to regulate immune responses.
2. When cells suffer metabolic stress, such as exercise or fasting, electrons leak from the ETC to form ROS, signalling to initiate adaptive responses.
3. ROS informs cells how to proliferate and differentiate correctly, guiding stem cells on how to develop, or to trigger wound healing.
4. Higher levels of ROS signal that irreparable damage has been caused to the functioning of the cell and initiate apoptosis, protecting the body from damaged cells persisting and multiplying.

This paints a more nuanced picture of ROS, whereby low amounts are necessary, slightly raised amounts signal stress and trigger adaptive responses, and higher levels initiate the death of malfunctioning cells. Too little ROS, known as reductive stress, can be just as problematic and may contribute to metabolic and cardiovascular disorders (Zhang et al., 2025).

Antioxidants

An antioxidant is a substance that helps to neutralise ROS and prevent oxidative stress. Herbs and spices rich in antioxidants have been used to prevent the spoilage of food and as medicines since ancient times (Embuscado, 2015) but upon the discovery of oxidation, they were initially employed for industrial applications: preventing the corrosion of rubber and metals, then to prevent the spoilage of oils and food (Cömert & Gökmen, 2018). When vitamin C and E were found in blood and urine samples in the 1950s, it was understood that antioxidants play a role in biology. Shortly afterwards, cells were observed to be producing antioxidant enzymes to manage oxidative stress (Di Meo & Venditti, 2020), creating two categories of antioxidants: those produced internally (endogenous) and those acquired externally (exogenous).

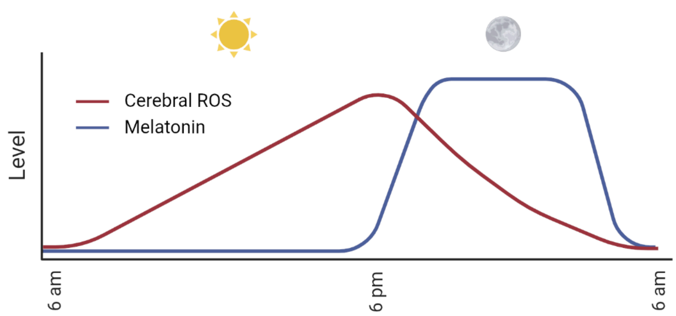
Endogenous Antioxidants

The first defence against ROS consists of enzymes produced by the mitochondria to protect itself. As the main site of superoxide production, they protect themselves with Superoxide Dismutase (SOD) that deradicalises superoxide ($O2^-$) by combining it with hydrogen protons (H^+) to form hydrogen peroxide (H_2O_2) and oxygen (O_2) (Fukai & Ushio-Fukai, 2011). While not a radical itself, hydrogen peroxide can cross membranes where it acts as a signalling molecule to indicate redox states (Bienert & Chaumont, 2014) and if not detoxified, reacts with other cellular components to form even more potent hydroxyl radicals (•OH) (Zhang et al., 2019). Therefore, hydrogen peroxide must be further transformed by other enzymes such as catalase (CAT), peroxiredoxins (Prxs), or glutathione peroxidases (GPx) which separate it into water (H_2O) and oxygen (O_2).

Another mechanism of antioxidant defence is mitohormesis (Palmeira et al., 2019). This is the process whereby mild perturbations in mitochondria are met with an adaptive response that leads to the production of more mitochondria, their reorganisation into fused networks (fusion) and the separation of old and damaged mitochondria (fission) where they are prepared for recycling (mitophagy). The end result is more mitochondrial antioxidant defences. Increases in ROS can trigger this response, as can a drop in ATP output, provided it is within acceptable limits.

Uncoupling refers to the action of a group of proteins that causes the electrons and protons to become “uncoupled” from the process of synthesising ATP and recombine into a hydrogen atom, with their energy released as heat. This maintains a core body temperature, but is also activated by elevated ROS to reduce its production (Zhao et al., 2019). Since it reduces ATP production, it can also initiate a mitohormesis response.

Some hormones play an important role in antioxidant defence. Melatonin is a powerful antioxidant and sleep regulator (Reiter et al., 2016), connecting redox states to circadian rhythms. The Free Radical Flux Theory of Sleep (Reimund, 1994) proposes that the animals sleep because consciousness is a very energy intense process that relies on oxygen. .



The Free Radical Flux Theory of Sleep and circadian melatonin cycles (image created in BioRender)

ROS that accumulates during wakeful consciousness is countered by melatonin which lowers consciousness while it detoxifies the brain. Failure to sleep results in oxidative damage, which can become irreversible over time, seen in neurodegeneration of the sleep deprived (Melhuish Beaupre et al., 2022)

Oestrogen has both direct action on scavenging radicals and upregulates endogenous antioxidant defences, enhancing the resistance of females to oxidative stress related diseases until menopause (Borrás et al., 2021). Many medicinal herbs contain phytoestrogens which can bind to oestrogen receptors, mimicking its antioxidant abilities (Borrás et al., 2010).

Melanin is a pigment which protects the skin against sun damage through both light absorption and radical scavenging (Menichetti et al., 2025). This pigment is also responsible for the colour of *hei zhi ma* (seed of *sesamum indicum*) and, although it does not have the same activity when consumed, it still upregulates many endogenous antioxidant pathways (Yang et al., 2023).

***Hei zhi ma* (seed of *sesamum indicum*), whose dark pigmentation derives from melanin Image courtesy of Phoenix Medical.**

Exogenous Antioxidants

Exogenous antioxidants are substances that are primarily acquired from our diet, or from medicines. Among them are vitamins and polyphenols, and instead of creating a list, which will be done later when we examine which herbs are antioxidants, this section will examine how they work, with examples of representative antioxidant compounds.

Radical scavenging is usually achieved by donating an electron or a hydrogen atom to the radical. This provides the unpaired electron with a partner of opposite spin, making the molecule stable and less reactive (Santos-Sánchez et al., 2019). The antioxidant, despite losing its electron or a hydrogen atom, is still less reactive and is often capable of being restored or broken down into a harmless form. This is the primary mechanism of ascorbic acid (vitamin C), which can do this twice before being broken down, or reduced back to its original state (Agwu, Ezihe & Kaigama, 2023). Tocopherol (vitamin E) also uses this mechanism but is lipid soluble (Rizvi et al., 2014) meaning they form a functional pair with vitamin C protecting the water based aspects of the cell, like the cytoplasm, and vitamin E protecting the lipid membranes. Additionally vitamin C can restore the radicalised vitamin E to its antioxidant state (Traber & Stevens, 2011).

Some antioxidants bind to an entire ROS molecule to form a radical adduct. Carotenoids, which are precursors to retinol (vitamin A), are one such group of antioxidants with lycopene, which makes tomatoes red, having a particularly high affinity for forming adducts with peroxyl radicals (Galano et al., 2009). This terminates the chain of reactions irreversibly but the resulting product is usually biologically inactive and cannot be regenerated, only degraded and excreted.

Ingested substances can also prevent the reactions that generate ROS. Chelation refers to a substance binding to metal ions, preventing their reaction with hydrogen peroxide to become potent hydroxyl radicals (McCarthy & Decker, 2022). Several polyphenols have metal chelating properties such as curcumin from turmeric (*jiang huang*, rhizome of *Curcuma longa*), epigallocatechin-3-gallate from green tea (cha ye, leaf of *Camellia sinensis*), and quercetin and myricetin found in many plant sources, accounting for the protective effects of polyphenol rich diets against Alzheimer's disease (Lakey-Beitia et al., 2021). Some warming spices can also prevent ROS formation by upregulating the expression of uncoupling proteins.

Some substances can act as electron acceptors, either removing the additional electron from a radical, or preventing its acquisition by oxygen. Recent research into glycyrrhizin, the main constituent of liquorice (*gan cao*, root of *Glycyrrhiza uralensis*), shows that it is capable of accepting electrons, preventing the formation of radicals (Ageeva et al., 2022). These are less researched but may be just as important, with some classical antioxidants being capable of switching between donor and acceptor status, depending on their environment (Becker, 2016).

***Gan Cao* (root of *Glycyrrhiza uralensis*), the source of glycyrrhizin, a potential electron acceptor. Image courtesy of Phoenix Medical.**

This influence of the environment means that some antioxidants can become pro-oxidants under the right conditions. Concentration, the presence of metal ions and the redox potential of the antioxidant can all influence this behaviour (Sotler et al., 2019). Vitamin C is pro-oxidant at high concentrations, and if vitamin E is not restored to its antioxidant state, it becomes a radical. Several polyphenols can also become pro-oxidant under the right conditions which vary according to different tissues (Perrone and D'Angelo, 2025). This means they could raise ROS in cancer cells, sensitising them to apoptosis induced by chemotherapy (Henley et al., 2017) and countering chemoresistance (Farhan, 2023), while protecting healthy cells from the same response (Fetoni, Paciello & Troiani, 2022). Dosing is challenging but research combining antioxidants with various chemotherapeutic and radiotherapeutic regimes seems promising (Singaravelan & Tollefsbol, 2025; Lu et al., 2025).

Measuring Antioxidant Potential

Much of the misinformation about antioxidants relates to the ways they are measured. These can be divided into chemical and biological tests, each with their own advantages and disadvantages.

Chemical methods involve mixing a known quantity of the antioxidant with a known quantity of a radical substance, or radical inducing mixture, and observing how much of the radical is quenched (Munteanu & Apetrei, 2021; Christodoulou et al., 2022). This is then Apetrei, 2021; Christodoulou et al., 2022). This is then compared to a known antioxidant, to calculate its relative potency. Some examples and their common abbreviations include:

- Oxygen Radical Absorption Capacity (ORAC) test: Peroxyl radicals are induced and their reduction is measured by a loss in fluorescence. A similar assay for hydroxyl radicals also exists (HORAC).
- Ferric Reducing Antioxidant Power (FRAP) test: A ferric ion complex (Fe^{3+}) is reduced to an intense blue ferrous complex (Fe^{2+}) in an acidic environment.
- Cupric Reducing Antioxidant Power (CUPRAC) test: The reduction of cupric (Cu^{2+}) to cuprous (Cu^{+}) at a neutral pH causes a colour change from light blue to orange.
- The Folin–Ciocalteu test: The total phenolic content (TPC) is measured through the action of phenolic compounds on the reagent in an alkaline state.
- ABTS test: This blue-green stable radical cation is reduced, indicating the Total Antioxidant Capacity (TAC) of a substance.
- DPPH test: The purple colour of this stable radical changes to pale yellow as it is reduced.

These tests are rapid and work with known mechanisms, informing us how the antioxidant works. However, the radicals used and conditions required for the reactions to take place are often not naturally occurring in biology, and they do account for effects on endogenous defences or bioavailability, so their biological relevance is questionable (Hollman et al., 2011; Granato, 2023). Regardless, these have made up the majority of research that reports on antioxidant capacity of herbs, which could mean a large discrepancy between the research literature and what is actually happening.

Biological tests measure oxidative stress using a reagent that enters the cells where it reacts with ROS and can be measured (Gardiner et al., 2020). Some examples include:

- DCFDA: This reagent enters the cells and is transformed by esterase enzymes into DCFH2 that reacts with cytoplasmic ROS to become DCF which emits a green fluorescence.
- MitoSOX: This reagent permeates the mitochondria to react with superoxide and produce a red fluorescence.

These tests have become increasingly popular in the last decade because they account for the complexity of how biological systems interact with a substance but cell cultures are much less predictable than chemicals so biological variability must be taken into account. Readings can also be distorted if the enzymes required to activate them are affected or the substances being researched can activate the fluorescence of the dye (de Haan et al., 2022). They also do not directly inform us of the mechanisms, but by blocking certain processes and repeating the experiment it is possible to determine the involvement of particular pathways.

The Problem of Antioxidants

One question that arises repeatedly is: are antioxidants actually good for us (Meffert, 2008; Berger et al., 2012)?

Soon after the initial hype of antioxidants, evidence emerged which challenged these claims. An eight year study of supplementing smokers with α-tocopherol and β-carotene found no change in the incidence of lung cancer and an increase in the risk of haemorrhagic stroke with an overall mortality rate 8% higher in the supplement group compared to control (ATBC-CPS group, 1994). A study looking at β-carotene and retinol supplementation in people with a high risk of lung cancer was stopped after only 21 months when initial data found 28% more lung cancers and 17% more deaths in the antioxidant group compared to control (Omenn et al., 1996).

It was not just cancer that antioxidants failed to prevent: an investigation into supplementation with vitamin E for 4.5 years in people with high risk of cardiovascular disease also found no apparent effect (HOPE study investigators et al., 2000) and a subsequent meta-analysis found high dose supplementation increased overall mortality (Miller et al., 2005). A Cochrane systematic review confirmed that antioxidants increased mortality, suggesting they should be considered medicinal products and undergo safety evaluation (Bjelakovic et al., 2012).

The exact reasons were not immediately apparent but recent discoveries regarding physiological roles of ROS explain this. ROS does lead to cancerous DNA mutations and enhance proliferation, but ROS is also the driving force behind apoptosis (Hayes, Dinkova-Kostova & Tew, 2020). Antioxidants could prevent this, promoting the survival of cancer cells (Harris & DeNicola, 2020; Dastmalchi et al., 2020). ROS is also an important signalling molecule to initiate exercise induced adaptive changes (Powers et al., 2020; Guan & Yan, 2022). Excessive antioxidant use can inhibit this response, lowering the benefits gained from exercise (Merry & Ristow, 2016; Pingitore et al., 2015; Mason et al., 2020) including the protective effects on cardiovascular and other diseases (Qiu et al., 2022).

Fortunately it seems these detrimental effects are only reported with isolated vitamins and high dose supplements. Diets high in vitamins and polyphenols still appear to be protective against many diseases (Jayedi et al., 2018). Herbal medicines lie between food and supplements, sometimes containing higher than average levels of antioxidants that are consumed routinely, so a consideration of antioxidant strategies within the Chinese medicine paradigm will follow.

Oxidative Metabolism in Chinese Medicine

Qi 氣 is often translated as "breath" and travels through the channels with the Blood, making some equate it to oxygen (Kresser, 2010), that binds to haemoglobin and facilitates cellular respiration. The *Nan Jing* chapter 8 describes the "moving qi (動氣 *dong qi*)" between the Kidneys as the "gate of inhalation and exhalation and … the origin of the Triple Burner (trans. Unschuld, 2016)." Chapter 36 links this to the Gate of Life (命門 *ming men*), creating the concept a flame within the Kidneys that is fanned by the Lungs, which act like bellows to control the rate of combustion. Combustion is an oxidation reaction, suggesting an early recognition that oxidative reactions are the driving force of life.

Oxidative Stress in Chinese Medicine

Su Wen chapter 5 implies that this combustion can be the source of life, or a source of harm:

"The qi of strong fire weakens. The qi of a small fire gains in strength. Strong fire feeds on qi. Qi feeds on small fire. A strong fire disperses qi. A small fire generates qi (trans. Unschuld & Tessenow, 2011)"

This implies that an appropriate level of oxidation generates useful energy (ATP), while intense oxidation not only fails to generate energy efficiently but even consumes and disperses it, leading to dysfunction, inflammation and disease.

Su Wen chapter 3 famously says that: "*Wind (feng 風) is the origin of one hundred diseases*." In ancient literature, qi referred to regular winds that brought consistent changes in weather and the seasons, while *feng* referred to unruly winds that caused disharmony and disease (Kuriyama, 1994). Here is another parallel, between qi and *feng*, as two movements of air that drive ordered or chaotic oxidative states.

Qi stagnation and Blood stasis are considered excess disorders, and if qi fuels oxidative metabolism, then excess qi implies oxidative stress. As Blood and qi function together, Blood stasis will also imply heightened oxidative stress. This parallels the role of iron in producing more potent species of ROS (Zhao, 2019) and the heightened states of oxidative stress haemoglobin causes during the early stages of a bruise (Jeney, et al., 2013).

Using this comparison, a more complete pathology of oxidative stress can be found in Zhang Jiebin's 1624 commentary to the Su Wen:

"*Wind is wood and generates fire. Excessive qi transforms into heat. The heat harms the yin. As a result the essence dissipates* (trans. Unschuld & Tessenow, 2011, footnote 62 to chapter 3)"

Zhang describes a mechanism where qi stagnation or wind (oxidative stress), if left unresolved, develops into heat (inflammation). Over time, this heat harms the yin.

First, it damages the fluids, developing into damp-heat (Clavey, 2003), before leading to yin deficiency and dryness (oxidative damage to cellular structures). If yin declines until it can no longer embrace yang then this too departs, resulting in symptoms of low energy, cold and dispersal of essence with shortened lifespan. Note a Five Phase sequence here: wind → heat → damp → dryness → cold. The equivalence of yang qi deficiency to diseases of mitochondrial senescence where ROS production increases and ATP decreases, such as chronic fatigue, metabolic and sleep disorders, dementia, and a predisposition to cancers has also been noted by other authors (Luo et al., 2022). In the *Baopuzi*, Ge Hong (4th century) advises that to live a long and healthy life, we should make the body adopt the properties of gold (Campany, 2002), a metal noted for its resistance to oxidation.

Antioxidants in Chinese Medicine

Chinese medicine categorises herbs and their properties through taste and colour, based on the Five Phase associations outlined in *Su Wen* chapters 5 and 22. These correspond to organoleptic properties which accompany many of the major antioxidants and relate them approximately to the stages of disease progression outlined by Zhang Jiebin.

Ascorbic acid (vitamin C) is found mostly in citrus fruits. In Chinese medicine the most common varieties include *Citrus aurantium (zhi shi / zhi qiao / zhi ke)* and *C. reticulata (chen pi / qing pi)* which are considered to be bitter and acrid, draining and dispersing accumulations of qi (Bensky et al., 2004). Acridity in this sense refers to their sharpness and a few other acrid herbs such as *la jiao* (fruit of *Capsicum* spp.) also have notable amounts of vitamin C (Kantar et al., 2016), sometimes more than 3 times that of oranges (USDA, 2019). Ascorbic acid is added to food as an antioxidant to preserve colour and freshness (Moncel, 2019) with lemon juice providing a natural way to achieve this effect (Conte et al., 2009), which supports the notion that this antioxidant helps to disperse excess qi and expel wind.

Carotenoids are pigments that give many red, orange and yellow vegetables their colour. They act as precursors to retinol (vitamin A), and are another major class of antioxidant molecules. Red relates to the Fire Phase, while yellow relates to the Earth Phase and the child of Fire, so it can be expected that many carotenoid containing herbs will clear heat. Some examples of heat clearing herbs that gain their red or yellow colour from carotenoids include *zhi zi* (fruit of *Gardenia jasminoides*; Ali et al., 2022), *ju hua* (flowers of *Chrysantemum morifolium*; Sharma et al., 2023), *jin yin hua* (flowers of

***Zhi Zi* (fruit of *Gardenia jasminoides*), that derives it red colour from carotenoids. Image courtesy of Phoenix Medical.**

Lonicerna japonica; Pu et al., 2020) and the flowers of *pu gong ying* (whole herb of *Taraxacum mongolicum*; Ko et al., 2023). *Gou qi zi* (fruit of *Lycium barbarum*) also acquires its red colour from carotenoids (Gao et al., 2017) and, despite being primarily categorised as a Blood and yin tonic, it is often used for consumptive disorders, where yin is harmed from heat and considered to have heat clearing properties of its own by Zhang Xichun (Bensky et al., 2004).

Sometimes carotenoids' colour can be masked by other pigments, such as chlorophyll in leafy green vegetables. These tend to be high in lutein, which has a particular role in protecting the eyes from phototoxic damage by absorbing blue light in the macula, along with its antioxidant activities (Buscemi et al., 2018), and is also preventative against stroke and cardiovascular disease (Li, Wu et al., 2021). Most taste bitter, which drains fire, and as green enters the Liver, we would expect these to clear heat from the Liver, whose pathology includes eye disorders and the stirring of internal wind, which is a common designation for stroke.

Tocopherol (vitamin E) is a group of lipid soluble compounds found primarily in the oil content of seeds. Some major sources in Chinese medicine include *xing ren* (seed of *Prunus armeniaca*; Pawar & Nema, 2023), *tao ren* (seed of *Prunus persica*; Landolsi et al., 2024), *hei zhi ma* (Mostashari & Mousavi Khaneghah, 2024), *huo ma ren* (seed of *Cannabis sativa*; Taaifi et al., 2021) and *hu tao ren* (seed of *Juglans regia*; Dai et al., 2024). While these have a diverse range of actions, seeds often act on the deeper parts of the body, having an affinity for the lower jiao, such as *xing ren* helping the breath to descend and *tao ren* moving Blood in the lower jiao. They also all have a moistening property, especially on the bowel, helping to restore or protect the yin. This corresponds to the role of vitamin E in protecting the lipid based structures in our cells from oxidation damage (Miyazawa et al., 2019) and preventing constipation (Cai et al., 2024).

Polyphenols are secondary metabolites abundant in plants and known for their antioxidant properties. They often have direct radical scavenging actions (Tsao, 2010) and more complex interactions with cellular signalling pathways that regulate endogenous defences and inflammatory responses (Rudrapal et al., 2022). Over 8,000 are described in the literature and some are also phytoestrogens. A thorough analysis is beyond the scope of this paper, but a few impart important properties to herbs relating to their actions and categories.

Anthocyanins are flavonoids with very strong radical scavenging abilities that give many foods a red, purple, blue, or black colour, depending on their concentration and environment (Alappat & Alappat, 2020). This colour spectrum suggests the *shaoyin* axis so they should benefit the Heart and Kidneys and research suggests they can improve cardiovascular health (Dong et al., 2022) and cognitive processing (Feng, Dong et al., 2023) to promote healthy ageing (Ma et al., 2025).

Black soybeans (*hei dou*; seed of *Glycine max*) obtain their dark colour from anthocyanins (Lakshmikanthan et al., 2024) and play an important role in the traditional processing of Kidney tonics. *He shou wu* (root of *Polygonum multiflorum*), *fu zi* (lateral root of *Aconitum carmichaeli*) and *wu tou* (root of *A. kusnezoffii*) gain their dark colour from steaming with black beans (Li, Chen & Zhang, 2024; Chen, Yong & Zhu, 2020). This guides their actions to the Kidneys, while also detoxifying them. Soybeans are also an important source of phytoestrogens which may provide additional antioxidant effects (Borrás et al., 2010).

Xing ren **(seed of *Prunus armeniaca*), a rich source of vitamin E. Image courtesy of Phoenix Medical.**

Hei dou **(seed of *Glycine max*), an important source of anthocyanins Image courtesy of Phoenix Medical.**

Some other Chinese medicines with an affinity for the *shaoyin* organs are naturally high in anthocyanins. These include *wu wei zi* (fruit of *Schisandra sinensis*; Jia et al., 2023), *sang shen zi* (fruit of *Morus alba*; Zhang et al., 2018), *shan zhu yu* (fruit of *Cornus officinalis*; Czerwińska & Melzig, 2018), *shi liu pi* (pericarp of *Punica granatum*; Abdelrahman et al., 2024) and *fu pen zi* (immature fruit of *Rubus chingii*). Only the immature fruit of *fu pen zi* is used in medicine, when the anthocyanin content is at its highest. As it ripens, these are replaced by carotenoids, and it is then used as food (Li et al., 2021). Most stabilise and bind (Bensky et al., 2004), preventing the leakage of *jing* and some also tonify the Kidneys which parallel the anti-ageing activities reported for anthocyanins. These examples also get their sourness from citric acid being their primary organic acid (Wang et al., 2024; Cui et al., 2025; Sobstyl et al., 2020; Bar-Ya'akov et al., 2019; Xiong et al., 2024), which is an essential fuel for mitochondria to produce the substrates required for oxidative phosphorylation. This may suggest that securing the essence is as much a combination of reducing oxidative damage with anthocyanins and providing mitochondria with necessary nutrients as it is about preventing physical leakage.

Resveratrol is another polyphenol famous for providing cardiovascular health benefits to red wine (Castaldo et al., 2019). It has a radical scavenging action on several types of ROS, prevents the formation of hydroxyl radicals through chelation of iron, upregulates endogenous antioxidant defences, downregulates inflammatory pathways and modulates oestrogen receptors with implications for cardiovascular disease, neurodegeneration, diabetes, cancer, osteoporosis and many other conditions related to ageing (Gu et al., 2021; Wada-Hiraike, 2021). However, it becomes a pro-oxidant under higher concentrations (Shaito et al., 2020). It is found abundantly in *hu zhang* (rhizome of *Polygonatum cuspidum*; Wang et al., 2013) which has the actions of invigorating the Blood, clearing Heat and resolving toxicity (Bensky et al., 2004).

Quercetin and kaempferol are bitter tasting flavonols found in many leafy greens and cruciferous vegetables (Cobos & Diaz, 2023). Quercetin is found abundantly in *huai hua* (flower of *Sophora japonica*), *huang qin* (root of *Scutellaria baicalensis*) and *sang bai pi* (bark of *Morus alba*), while both are found in *yin xing ye* (leaf of *Ginkgo biloba*), *cha ye, hong hua* (flowers of *Carthamus tinctorius*) and *xiang fu* (root of *Cyperus rotundus*) (Cherian et al., 2025; Alexander, Parsaee & Vasefi, 2023). These are often cold and bitter in taste and have heat clearing and qi and Blood invigorating properties.

***Hu zhang* (rhizome of *Polygonatum cuspidum*), a source of resveratrol.**
Image courtesy of Phoenix Medical.

Both have been found to have hormetic effects due to their potential to auto-oxidise which can act as a signal to activate endogenous antioxidant mechanisms at low doses, but become pro-oxidant at higher doses (Calabrese et al, 2024; Calabrese et al., 2025).

Curcumin is a polyphenol that gives *jiang huang* its brilliant yellow colour and is taken by many for its antioxidant and anti-inflammatory activities. These involve both direct scavenging activity, the upregulation of innate antioxidant enzymes and modulation of inflammatory cytokines (Dehzad et al., 2023). In Chinese medicine, *jiang huang* invigorates qi and Blood and expels wind (Bensky et al., 2004). It also inhibits melanin synthesis and has a pro-oxidant effect when exposed to blue light (Wolnicka-Glubisz & Wisniewska-Becker, 2023). This is not an issue when used in its natural form due to low bioavailability, but may become a problem with extracts that are modified to improve their absorption, or when used topically if left uncovered.

Berberine is an alkaloid that imparts the infamous bitterness to many Chinese medicines. It is found in bitter, yellow herbs such as *huang lian* (rhizome of *Coptis chinensis*), *huang bai* (bark of *Phellodendron amurense*) and *yan hu suo* (root of *Corydalis yanhusuo*). It has many antioxidant mechanisms, both through direct scavenging and by upregulating endogenous cellular mechanisms and may be useful in cardiovascular disease, diabetes, neurological disorders, inflammation and infections (García-Muñoz et al., 2024; Askari et al., 2023; Feng, Chen et al., 2023). *Huang lian* and *huang bai* are both bitter, cold and drain damp-heat. *Yan hu suo* has similar properties to *jiang huang,* being bitter, acrid and warm, and shares its actions of regulating qi and Blood.

Melatonin was mentioned above as a powerful antioxidant hormone and circadian redox regulator. Chen et al. (2003) found the highest levels in *chan tui* (moulting of *Cryptotympana pustulata*), *zi hua di ding* (herb of *Viola philipica*), *gou teng* (branchlets of *Uncaria rhynchophylla*), *sang ye* (leaf of *Morus alba*), *huang bai*, *sang bai pi, huang lian* and *da huang* (root of *Rheum palmatum*), all having over 1000 ng/g. These herbs are all cooling and have actions to clear heat and subdue or expel wind (Bensky et al., 2004), the violent manifestation of qi.

Many spices that invigorate the yang and dispel internal cold contain aromatic compounds that provide their hot taste. Several of these have been observed to upregulate the expression of uncoupling proteins, which reduce ROS production and generate heat, but at the expense of reduced ATP synthesis. This can then trigger a mitohormesis response resulting in improved mitochondrial function, the browning of adipose tissue and improved metabolic health (Kwan et al., 2017). Some examples include eugenol in *ding xiang* (fruit of *Syzygium aromaticum*; Usta et al., 2002), cinnamaldehyde in *rou gui* and *gui zhi* (bark and branchlets of *Cinnamomum cassia*; Li et al., 2021; Zuo et al., 2017), 6-shogaol and 6-gingerol in *sheng jiang* and *gan jiang* (fresh and dried rhizome of *Zingiberis officinale*; Sampath et al., 2021) and capsaicin in *la jiao* (Baskaran et al., 2016; Panchal, Bliss & Brown, 2018; Abdillah & Yun, 2024). This places them in a different category to most of the antioxidants discussed so far, being warming tonics instead of dispersing and heat clearing. They are often paired with the anthocyanin rich herbs, which also share properties of strengthening and stabilising the Kidneys. These two groups are most indicated in the depleted stages of the cycle, to counter deficiency of the Kidneys and the fundamental polarity that is at the source of life.

Chinese medicine does not prescribe isolated constituents, so there will be plenty of exceptions to these examples which should be seen as trends and not fixed rules. Most herbs will have multiple antioxidants and other constituents affecting its action. One example is the orange colour of mature citrus fruits coming from carotenoids (Saini et al., 2022) which, combined with their bitter taste, means that they should clear heat, yet they do not (Bensky et al., 2004). One answer is that qi stagnation will generate heat so regulating qi does clear heat indirectly by removing its source, and is indicated by the ability of citrus fruits to transform phlegm, which is generated by stagnant heat damaging fluids and may be resolved by regulating the qi (Clavey, 2003).

Prescribing Antioxidants in Chinese Medicine

The final point to address is whether there is any classical guidance on when to prescribe antioxidant rich herbs. *Nan Jing* chapter 81 says:

"Do not replenish a repletion or deplete a depletion - [that is] weaken what is insufficient [or] add to any existing surfeit (trans. Unschuld, 1986)."

This simple piece of advice appears to explain what has been discovered about antioxidants: If we wish to get stronger, we should avoid the reducing antioxidants that regulate qi and Blood, or clear wind and heat, and turn to those that nourish the Kidneys, warm yang and stabilise the essence. Even the reports on antioxidant effects on exercise suggest that we should not be reducing athletes prophylactically, lest we inhibit their ability to develop from their training. In the early trials that reported increased mortality from antioxidants, we can speculate that they were depleting the depleted, and can ask whether the same effect would be seen if they were prescribed differently. In complex and chronic cases, as the diseases being trialled were, a combination of reducing and tonifying antioxidants that work to strengthen their mitochondrial health may have produced different results to the high dose vitamins used, as many trials of polyphenols now indicate they could.

For clinical guidance, it seems clear: there is no blanket antioxidant strategy. Use the bitter, cold and reducing antioxidants when the patient is experiencing an excess, and warm, tonifying and astringent herbs when they are deficient. Complex patterns require mixed strategies. The prescription should always be guided by their current state of health and activity levels, and extra caution may be required if they are taking high dose antioxidant supplements along with their herbs.

Conclusion

This has been a deep dive into the world of free radicals and antioxidants, their truths and their myths, and their relationship to Chinese medicine. It has covered what radicals are, what roles they play in physiology and pathology, and how best to use them to treat patients. The main point is that the territory is not as black-and-white as advertising campaigns would have us believe. Radicals are necessary for our regular functioning and antioxidant supplementation has often failed to achieve the results that have been promised. In some cases, they may even be harmful. Chinese medicine appears to have addressed this in the language of qi stagnation generating heat leading to damage to yin, and loss of yang and essence, providing some simple guidelines based on pattern differentiation and the tastes, colours and properties of herbs.

In the next instalment of this series, there will be a discussion of another major class of herbs that act on mitochondria: adaptogens.

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