Chapter 1

INTRODUCTION

This chapter sets the background for the thesis work. A brief description about the public health issues like population ageing and iron deficiency anemia (IDA), the role of nutrition in combating these health issues and the need for research in holistic nutrition like Ayurvedic Rasayana are summarized. The specific objectives and thesis overview are also described.

1.1 Population ageing, a public health problem

Ageing is defined as a continuous process that includes loss of functional capability and the increase in risk of disease and death (Franco et al., 2009). World Health Organization (WHO) statistics indicate that the human population is progressively ageing (United Nations, 2013). Decrease in the mortality and fertility rate of individuals has been contributing to the addition of older individuals to the world population (Turner, 2009). The global share of older people (aged 60 years or over) was 11.7% in 2013 and is expected to reach 21.1% by 2050 (United Nations, 2015). Even though the incidence of infectious and parasitic diseases has decreased to a significant extent, the burden of non-communicable diseases (NCD) has increased drastically. Ageing, diet and life style changes have been contributing to the development of NCD’s like cancer, cardiovascular diseases, diabetes, Alzheimer’s disease, Parkinson’s disease and dementia (Salive and Guralnik, 1997). This increases the burden of health care costs and decrease productivity. Thus, health care of ageing population poses major social and economic consequences.
1.2 Active ageing

Public health agencies and geriatrics researchers have started focusing on “active
ageing” or “healthy ageing” or “successful ageing”. WHO defines active ageing as the
process of optimizing opportunities for health, participation and security in order to
enhance quality of life as people age (WHO, 2002). A ‘healthy ageing phenotype’ can
be defined as ‘the condition of being alive, while having highly preserved functioning
metabolic, hormonal and neuro-endocrine control systems at the organ, tissue and
molecular levels (Lara et al., 2013).

Active ageing allows people to realize their potential for physical, social, and mental
well-being throughout the life course and to participate in society, while providing
them with adequate protection, security and care when they need (WHO, 2000). Focus on active ageing is also said to improve ‘longevity dividend’, which is defined as "the sum of health, social and economic benefits that result from slower ageing” (Olshansky et al., 2007). Researchers indicate that the investments and interventions for healthy ageing would have greater effect on quality of life than compared to disease specific treatment approaches (Kaeberlein et al., 2015).

1.3 Nutrition for wellness and healthy ageing

Wellness is defined as the state of being in good health. Focus of health care has
shifted from disease centric to wellness. It is widely accepted that healthy living is not
just a ‘fate effect’ but a result of interweaving between behavioral, environmental and
genetic factors (Boccardi et al., 2016). In this context nutrition and life-style are the
behavioral determinants of healthy ageing. Optimal nutrition plays a significant role
in determining the wellbeing of young, delay age related degeneration and reduce the
risk of contracting disease (World Health Organization, 2002). The current literature
evidence suggests that diet composed of fruit, vegetables, fish, whole grains and starchy low-fat staple foods are likely to play a key role in promoting aspects of wellness and healthy ageing including life expectancy (Jong et al., 2014). This dietary pattern is also shown to lower risk of cardio-metabolic diseases and adverse cognitive outcomes.

Molecular studies have shown that irreversible ageing phenotype arises because of the accumulation of macromolecular damage within the cell (Richardson and Schadt, 2014). Several nutritional components including primary and secondary metabolites of plants have been experimentally shown to reduce such damage, or enhance the organism's capacity to repair the damage, leading to reduced risk of age-related diseases and extended longevity (Mathers, 2015). An optimal intake of micronutrients and metabolites is also said to impart metabolic harmony, which in turn prevents disease and imparts wellness (Ames, 2003).

1.4 Iron deficiency anemia (IDA) – another public health issue

Iron is an essential micronutrient, as it is required for adequate erythropoietic function, oxygen transport, oxidative metabolism, DNA synthesis and cellular immune responses (Munoz et al., 2009). Human body does not have mechanism to synthesize iron, so diet is the only source of iron for all physiological requirements. Systemic iron status in the organism is maintained by regulation of iron absorption and storage, but there is no known regulated mechanism for iron excretion from the body (Siah et al., 2006). Increased iron requirements, limited external supply and increased blood loss may lead to iron deficiency (ID) and iron-deficiency anemia (Gomollon and Gisbert, 2009).
Iron deficiency anemia (IDA) affects more than 2 million people worldwide (Kassebaum et al., 2014). The reported prevalence indicates that globally about 40% of pre-school children, 30% in reproductive age women and 38% of pregnant women suffer from iron deficiency (Camaschella, 2015). IDA affects cognitive development, immunity, physical productivity and increased morbidity (Lopez et al., 2016). Maternal mortality and low birth weight are observed in pregnancy linked IDA (Bond, 2016). For the past several decades, governments and WHO has been trying various intervention strategies to combat IDA. Prescribing iron rich foods, distribution of iron-folic acid tablets, fortification of commonly consumed food materials are some of the strategies adopted (Walter et al., 1993; Sloan et al., 2002; Thuy et al., 2003; Zimmermann et al., 2003). But, these interventions have not made a significant impact in reducing IDA. The major reason behind the failure of iron supplementation programmes could be the lesser bioavailability of iron (Nair and Iyengar, 2009). Researchers have been focusing on iron bioavailability enhancers. Ascorbic acid (Cook and Reddy, 2001) and Na-EDTA (Thuy et al., 2003) are some of the iron bioavailability enhancers. Adding them with iron salts can decrease palatability and aggravate side effects like nausea and vomiting (Galloway and McGuire, 1993; Ekstrom et al., 2002).

1.5 Need for research in holistic nutrition

Modern biomedicine does not emphasize the significance of nutrition as a major cause of a wide range of health disorders. Subsequent to infliction with disease, it relies more on target specific drug preparations to re-orient physiology. But, any deviation from the normal might have caused several molecular changes in the complex network of human body. For example, in the case of IDA, iron deficiency may not
just be due to iron unavailability but may also be due to lack of the potential to absorb iron in the system. In the latter case, supplementation of iron may not make any impact. Optimizing the system and its absorbing capacity should be the prime motive.

Similarly, in the case of ageing, several debilitative conditions converge. Rather than individually treating each of the chronic diseases, it would be better if we can directly target ageing. While targeting such complex phenotypes, a holistic nutrition can play a very vital role. Such nutrition can normalize and optimize the system as a whole, rather than looking at specific targets.

Holistic nutrition is an approach to develop a healthy balanced diet while taking into account the person as whole. The goal of holistic nutrition is to facilitate a complete recovery plan as well as build a strong body for lifelong optimal health. There is a need to look at novel and innovative solutions that can address all aspects of wellbeing and which are sustainable.

### 1.6 Rasayana for wellness

Ayurveda is a traditional medical system of India. Treatment principles of Ayurveda are based on the whole system approach and gives equal importance to the individuals, food and medicine. One of the eight disciplines of Ayurveda, called Rasayana is specifically for rejuvenation (Udupa, 2004). The Rasayana tantra includes some common good living practices and use of herbal or herbo-mineral preparations for wellbeing of an individual (Payyappallimana and Venkatasubramanian, 2015). They have been in practice for several thousands of years but the exact mode of action of the Rasayanas based on Ayurvedic principles has not been studied except for few a general bioactivity studies (Balasubramani et al., 2011).
It was hypothesized that understanding Rasayana concept and studying the selected aspects and mode of action will add new dimension to the science of rejuvenation particularly in ageing and nutrition related disorders like IDA. The findings of such study will help in development of low-cost, plant-based easily acceptable interventions for IDA and also for healthy ageing and wellness using pomegranate, which is mentioned as Rasayana in Ayurveda.

1.7 Objectives of the study

With the above hypothesis, the following were fixed as the objectives of this study:

(i) To understand the logic behind the functioning of Ayurvedic Rasayana products

(ii) To develop appropriate in vitro and in vivo models to study dadima Rasayana for iron deficiency anemia (IDA)

(iii) Scientific validation of the use of dadima Rasayana for wellness

1.8 Thesis overview

Chapters in the current thesis have been laid out as below. The methodology, findings and discussions are self-contained in each chapter.

Chapter 2 - Methodology: Overall trans-disciplinary research approach followed in understanding the concept of Rasayana by theoretical and experimental studies using dadima Rasayana are presented in this chapter.

Chapter 3 - Review of Literature: This chapter introduces the biomedical aspects of wellness, ageing and iron deficiency anemia (IDA), followed by literature review on the models used for ageing and iron metabolism related studies. A detailed review on the current status of research on pomegranate also forms a part of this chapter.
Chapter 1

Chapter 4 - Rasayana and its role in the management of ‘Pandu’ and ‘Svasthya’: This chapter is a review of classical Ayurveda literature and also recent texts to understand the Ayurvedic concepts of Rasayana, Pandu, Svasthya and also the Dravyaguna (Ayurveda pharmacology) of Dadima.

Chapter 5 - Chemical Standardization of Pomegranate juice: This chapter describes the preparation and standardization of pomegranate juice (PJ) used for experimental studies. Phytochemical standardization, total dissolved solids (TDS), total soluble solids (TSS), total phenolics, total acids, ascorbic acid content and iron content in PJ are presented.

Chapter 6 - PJ increases iron bioavailability and uptake in in vitro models: The models selected and experiments performed to study the agni enhancing property of PJ with reference to iron bioavailability and uptake are presented. Cell free and cell based (Caco-2 and HepG2) in vitro models have been used.

Chapter 7 - PJ improves iron status and ameliorates iron deficiency induced cellular changes in Saccharomyces cerevisiae: Experimental studies performed to understand the panduhara and dhatuposhana properties of PJ with reference to improving iron status, heme content, ATP content and healthy mitochondria in anemic yeast (Saccharomyces cerevisiae) cells are summarized.

Chapter 8 - PJ enhances healthy lifespan in Drosophila melanogaster: Experiments conducted in D. melanogaster model to study the effect of PJ on lifespan extension (ayuvardhana), delay ageing (vayasthapana), immunity (vyadhikshamatva) and reproductive potential (vrshya) are described. The possible molecular mechanisms for longevity have also been explored.
Chapter 9 - Conclusions: Overall summary and future directions for Rasayana research are presented in this chapter.
1.9 References


World Health Organization, Tufts University School of Nutrition Science: Keep fit for life. Meeting the nutritional needs of older persons. 2002.