Advanced Glycation End Products (AGEs) are produced in the body via several mechanisms, including protein cross-linking ability. The formation of AGEs also results in resistance to proteolytic degradation, especially in long-lived proteins (Suarez et al., 1995; Jung et al., 2014). The result is increased persistence of tissues damaged by AGEs. AGEs may also disrupt cellular functions by altering the functions of intracellular proteins. The binding of AGEs to their specific cellular receptors (RAGE) initiates transcription of Nuclear Factor kappa beta (NF-κB). This results in increased expression of pro-oxidant and pro-inflammatory genes, as well as the production of additional RAGE, all of which promote accelerated AGE formation (Brownlee, 2001; Ramsey et al., 2012).

AGE accumulation rates tend to increase as we grow older. A positive correlation between concentrations of various AGEs and chronological age has been reported by numerous researchers and is observed in various tissues. A few examples include the lens of the eye, the macula, knee cartilage, arteries, lung tissue and the skin (Araki et al., 1992; Dyer et al., 1993; Schleicher et al., 1997; Ishibashi et al., 1998; Verzijl et al., 2000). It is apparent that increased AGE concentrations throughout the body contribute significantly to the aging process (Semba et al., 2010).

Chronic health conditions, such as diabetes, may increase the rate of AGE accumulation (Ramasamy et al., 2005). However, numerous lifestyle-related factors are also associated with increased AGE accumulation. Tobacco use is a particularly strong predictor of elevated AGEs (Cerami et al., 1997). The presence of metabolic syndrome and central adiposity are also associated with elevated AGEs, which also may be due to impaired glucose tolerance (Monami et al., 2008; Smit et al., 2013). Diet also impacts AGEs levels and elevated blood glucose has long been known to be an important factor for increased AGE formation (Brownlee et al., 1984). Therefore, strategies which help to control blood glucose levels will also be useful in controlling AGE levels within the body.

Weight management improves glucose tolerance (Lloret-Linares et al., 2008). Additionally, reducing the absorption of carbohydrates in our diet may also help regulate blood glucose levels. Limiting the conversion of starch to absorbable monosaccharides may result in both weight loss and regulation of blood glucose. White
kidney bean (*Phaseolus vulgaris*) extract has been demonstrated in human trials to help reduce body mass in overweight and obese adults and improve postprandial glycemic control (Udani and Singh, 2007; Barrett and Udani, 2011). The extract is able to produce these effects through inhibiting α-amylase, an enzyme which breaks down starch into absorbable monosaccharides (Marshall and Lauda, 1975). Dietary fiber intake also is reported to have positive effects on body weight, metabolic syndrome and blood glucose (Papathanasopoulos and Camilleri, 2009). Additionally, white kidney bean extract, β-carotene and noni fruit (*Morinda citrifolia*) have been found to possess antiglycation activity (Aruna et al., 1999; Pari and Venkateswaran, 2003; Kusirisin et al., 2009; Gacche and Dhole, 2011). Considering the background data, the current study was designed and conducted to investigate the efficacy of daily ingestion of a combination of white kidney bean extract, dietary fiber, β-carotene and noni fruit pulp in reducing AGE levels and body mass.

**MATERIALS AND METHODS**

Thirty adult volunteers were enrolled in this trial. Participants included males (n = 9) and females (n = 21) who ranged in age from 28-69 years. Those included had a Body Mass Index (BMI) of at least 24. Study participants were instructed to consume one daily serving of a commercially available combination of white kidney bean extract, dietary fiber, β-carotene and noni fruit pulp (TruAge Sugar Stop, Morinda, Inc., Provo, Utah, USA) immediately prior to consuming their largest meal of the day. This regimen was followed for 77 days (11 weeks). Participants were asked to record their food intake and track daily caloric intake using a website service or mobile device app, such as My Fitness Pal (MyFitnessPal Inc., San Francisco, California, USA) and Lose It! (FitNow, Inc., Boston, Massachusetts, USA). Using these services, each participant was instructed to adjust their daily calorie intake to achieve weekly weight loss goals that did not exceed 0.9 kg/week. They were also asked to exercise at least three times per week, with the specific type and duration left to the discretion of the individual. Informed consent was obtained from each participant.

Body mass was measured at the initiation of the study (day 0) and then weekly, thereafter. Weekly weight changes from baseline values were calculated and the average weekly weight change per person, as well as standard deviation, were determined for each week. Average weight was compared against day 0 using Student’s t-test. Fat mass was also measured by a validated bioelectrical impedance method with the SC-331S Body Composition Analyzer (Tanita Corporation of America, Inc., Arlington Heights, Illinois, USA) at the same time as body mass was measured, as described in previously reported studies (Ritchie et al., 2005; Ramsey et al., 2012). Fat mass changes were also compared statistically with Student’s t-test.

Advanced glycation end product measurements were made with the TruAge scanner, a consumer version of the AGE Reader mu (Diagnoptics Technologies B.V., Groningen, Netherlands). The scanner uses the principle of skin auto-fluorescence to measure AGE levels and is based on clinically validated methods (Meerwaldt et al., 2004). Each participant was instructed to not apply any lotions or skin treatments to the volar side of the forearm for at least one day prior to measurements with the scanner. Initial (day 0) and final (day 77) AGE measurements were made on a site of the volar forearm that was approximately 10 cm from the fold of the elbow. The TruAge scanner provides an AGE score, which is based on the intensity of skin auto-fluorescence through the 420-600 nm range, following excitation through the 300-420 nm range. Skin auto-fluorescence has been correlated with chronological age in multiple population studies (Koetsier et al., 2010; Yue et al., 2011; Simon Klenovics et al., 2013). Using a linear equation derived from the regression analyses in the studies, the AGE score can be used to calculate an age in years that corresponds to the intensity of skin auto-fluorescence. This is defined as the TruAge. Differences were calculated between each person’s actual age in years and the calculated TruAge (defined as TruAge difference). A positive TruAge difference value indicates that an individual has higher AGE levels than expected for their chronological age, based on the trends observed in population studies. A negative TruAge difference indicates that a person has lower AGE levels than expected for his or her chronological age. Significant changes in AGE scores and TruAge difference values were evaluated with Student’s t-test.

**RESULTS AND DISCUSSION**

The average weekly change in weight, as compared to baseline values, is described in Fig. 1. There were consistent changes in weight throughout the 11 week period. The average weekly weight loss was 1.3 kg, which was 0.4 kg (or~0.9 Pounds) more than the 0.9 kg target of the daily calorie intake restriction. Mean weights were significantly different from the baseline mean at each subsequent week (p<0.0001). Fat mass also was reduced significantly. Mean fat mass, ±S.D., declined from 19.1±3.38 kg on day 0 to 17.5±3.41 kg by day 77 (p<0.00001).

Changes in AGE measurements are described in Table 1. Mean AGE score declined by 10.6% from the initial value on day 0. Even so, AGE levels tend to increase with chronological age. As such, TruAge difference is a more accurate measurement for comparison since it controls for the effects of chronological age. The average TruAge difference on
day 0 was 2.33 years. This indicates that this group of participants had elevated AGE levels when compared against healthy population trends. Afterwards, all participants experienced a decline in TruAge difference. The minimum decline was 2 years, with the maximum being 20. By day 77, all participants had AGE levels that either matched expected values for their age or had levels that were expected for people younger than themselves. After 11 weeks, mean TruAge difference declined significantly to −6.5 years, which indicates that this group had much lower AGE levels than expected among the healthy general population. In terms of AGE associated years, this is an average decline of 8.83 years.

The results of this pilot study are consistent with data presented in previous reports. As discussed above, lifestyle factors and health status influence AGE accumulation. In type 2 diabetes, skin autofluorescence not only increases with hyperglycemia and age but also with the presence of abdominal obesity (Monami et al., 2008; Den Engelsen et al., 2012). Not only is obesity a predictor, but increased BMI is also a determinant of skin auto-fluorescence (Lutgers et al., 2006). Therefore, it is very reasonable that positive changes to body composition are likely to result in similar changes to AGE levels. One reason for this is that oxidative stress is enhanced by central obesity (Urakawa et al., 2003; Furukawa et al., 2004; Silver et al., 2007). As oxidative stress is also a promoter of AGE formation (Araki, 1997; Miyata et al., 1997), reduction in fat mass should contribute to a reduced pro-oxidant environment within the body. Within the context of oxidative stress, it is important to note that β-carotene, a natural nutrient found in plant foods, has well known antioxidant properties (Bendich, 2004). Noni fruit juice also possesses significant antioxidant activity (Wang et al., 2009, 2013), although a minor component of the combination product.

Reduction in sugar absorption by the white kidney bean extract is also an important consideration in the reduction in AGE levels. As stated above, supplementation with this extract in human trials reduced the body mass of overweight and obese adults and improved post-prandial glycemic control. Glycemic control is a key factor in controlling AGE accumulation, as blood sugar concentration is a limiting step in this process (Forbes and Cooper, 2013). As discussed previously, ingestion of dietary fiber appears to decrease postprandial glucose levels (Babio et al., 2010). Therefore, it contributes to the observed results by also improving glycemic control. Further, exercise is very effective in controlling blood glucose and ≥30 min/day for at least 3 day/week has been associated with lower skin auto-fluorescence levels (Simon Klenovics et al., 2013). Even when adequate glycemic control has been reached, the demonstrated anti-glycation activity of β-carotene, noni fruit and white kidney bean extract should also help curb AGE accumulation.

**CONCLUSION**

The results of this open-label clinical trial indicate that the daily use of a combination of white kidney bean extract, dietary fiber and noni fruit pulp, along with calorie restriction and exercise, improves the AGE load in the body, reduces body weight and improves lean body composition. The presumed decrease in sugar intake, as well as improved glycemic control, contributes to the lower rate of AGE accumulation, resulting in improved overall health and a reduction in AGE associated years. As such, the intervention evaluated in this study may be useful as an anti-aging strategy.

**REFERENCES**


