throughout the cytoplasm. Interestingly, Golgi complexes in placebo+CC14 group contain small low-density vesicles. Golgi complexes in the processed *Morinda citrifolia* products+CC14 group contain large vesicles with increased electron density, and Golgi cistemal stacks were well developed. Those in the placebo+CC14 group were often swollen and diminished.

[0070] Possible mechanism of the cancer preventative effect of processed *Morinda citrifolia* products were studied. Female SD rats were divided into two groups of six each. The control group was given regular drinking water and rat show, ad libitum. The processed *Morinda citrifolia* products group was given 10% processed *Morinda citrifolia* products in drinking water and rat chow, ad libitum. One week later, three animals from each group received intragastrically 25 mg/kg of DMBA containing 5% dimethysulfoxide in corn oil. All animals were sacrificed 24 h later. DNA was isolated from liver, lung, heart, and kidney. The DNA adducts were analyzed by P-postlabeling technique. After one week of consumption, the processed *Morinda citrifolia* products group showed a reduction in both the number and level of DMBA-DNA adducts from each of the four organs studied. The quantitative estimate after radioactive counting indicated that processed *Morinda citrifolia* products reduced the amount of DNA adduct formation by 80% in kidney, 42% in liver, 41% in lung, and 26% in heart. Even more dramatic experimental results were obtained using male C57 BL-6 mice. Processed *Morinda citrifolia* products were able to reduce the formation of DMBA-DNA adducts by 90% in kidney, 70% in liver, 60% in heart, and 50% in lung. This is the first finding of the cancer preventive effect at the initiation stage of carcinogenesis by processed *Morinda citrifolia* products. This data indicates that processed *Morinda citrifolia* products may prevent cancer at the initiation stage of carcinogenesis.

[0071] In order to explore the mechanisms of the cancer preventive effect of processed *Morinda citrifolia* products, the antioxidant activity was examined. The study was designed to measure how well processed *Morinda citrifolia* products scavenged superoxide anion radicals (SAR) and quenched lipid peroxides (LPO) by TNB assay and LMB assay, respectively. SAR scavenging activity was examined in vitro by tetrazolium nitroblue (TNB) assay. In TNB assay, SAR reduces TNB into formazan blue, which absorbs at 602 mm. A SAR scavenger, such as processed *Morinda citrifolia* products, reduces the absorbency by reacting with SAR. In this assay, a standard curve is produced when SAR are generated from NADH under aerobic conditions, with phenazine methosulfate as a catalyst. In LMB assay, LPO oxidizes leucomethylene to methylene blue in the presence of hemoglobin. The resultant blue color can be quantified spectrophotometrically at 660 nm.

[0072] In vitro processed *Morinda citrifolia* products showed a dose-dependent inhibition of both LPO and SAR. The SAR scavenging activity of processed *Morinda citrifolia* products was compared to that of three known antioxidants: Vitamin C, grape seed powder, and Pycnogenol at the daily dose per serving level recommended by US RDA's or manufacturer's recommendations. Under the experimental conditions, the SAR scavenging activity of processed *Morinda citrifolia* products was shown to be 2.8 times that of vitamin C, 1.4 times that of Pycnogenol, and 1.1 times that of grape seed powder. Therefore, processed *Morinda citrifolia* products has a great potential to scavenge reactive oxygen free radicals.

[0073] Carbon tetrachloride is a liver carcinogen and lipid hydroperoxidation inducer. To further confirm the antioxidant activity of processed *Morinda citrifolia* products in vivo, a carbon tetrachloride induced liver injury model in female SD rats was selected. Ten percent of processed *Morinda citrifolia* product in drinking water for 12 days was able to reduce the liver LPO and SAR levels to 20% and 50% of that observed in the placebo group 3 hours after CC14 administration. In conclusion, processed *Morinda citrifolia* products may protect liver from an extrinsic carcinogenic CC14 exposure.

[0074] Antioxidants in processed *Morinda citrifolia* products may protect individuals from cigarette smoke by scavenging oxygen free radicals and quenching lipid peroxides. In order to examine this hypothesis, a one-month double blinded, randomized, and placebo-controlled clinical trial was designed to test the protective effect of processed *Morinda citrifolia* products on plasma SAR and LPO in current smokers. The subjects were supplemented daily with two ounces of processed *Morinda citrifolia* products (n=38) or placebo (n=30), twice a day for 30 days. The plasma SAR and LPO levels were determined before and after trial by TNB and LPO assay, respectively. There was no effect observed on plasma SAR (0.23±0.15 versus 0.21±0.17 μmol/mL) and LPO (0.58±0.22 versus 0.59±0.21 μmol/mL, $P<0.05$), respectively. These results indicate that processed *Morinda citrifolia* products may protect individuals from oxidative damage induced by tobacco smoke. Smoking specific, lipid peroxides and the related decomposed products such as malondialdehyde, induced DNA adducts will be analyzed soon.

[0075] The data from the in vitro study, CC14-induced liver injury model of female SD rats, and current smokers indicate that processed *Morinda citrifolia* products is a strong antioxidant which can scavenge reactive oxygen free radicals and quench lipid hydroperoxides, therefore reducing the cancer risk.

EXAMPLE THREE

Anti-Inflammatory Action and Selective COX-2 Inhibition by Processed *Morinda citrifolia* Products

[0076] In this study, the selectivity of COX-2 inhibition of processed *Morinda citrifolia* products versus COX-1 in vitro was investigated. The inhibitions of processed *Morinda citrifolia* products on COX-2 and COX-1 activities were compared with that of the traditional NSAIDs such as Aspirin, Indomethacin, and a known selective COX-2 inhibitor, Celebrex. The COX-1 and COX-2 activities were determined based upon the PGE2 levels generated during the incubations of human platelets with tested compounds and/or vehicle by the Amersham ELA assay. The IC of processed *Morinda citrifolia* products, Aspirin, Indomethacin, and Celebrex on COX-1 are 5%, 4.55 μmol/L, 0.01 μmol/L, and 1.4 μmol/L, respectively, and that for COX-2 are 3.8%, 595 μmol/L, 0.4 μmol/L, and 0.47 μmol/L respectively. The data was converted into a ratio of IC_{50} COX-2/COX-1. It was 0.76 for processed *Morinda citrifolia* products, 119 for Aspirin, 40 for Indomethacin, and 0.34 for