This review summarizes the literature on different pharmacological effects, phytochemical analysis and various other applications of *Anacardium occidentale* L. (Cashew). *Anacardium occidentale* is a medicinal plant reputed in folk lore system of medicine in tropical countries, and of which the pharmacological activities have been scientifically demonstrated. The review of literature reflects the plant parts involved, the nature of the extracts used and the names of the active principles.

### 4.1 SCIENTIFIC REPORTS PUBLISHED FOR LEAVES OF CASHEW

1. **Antiulcerogenic activity:** The antiulcerogenic effect of a hydroethanolic extract of *Anacardium occidentale* L. leaves was investigated. The extract inhibited gastric lesions induced by HCl/ethanol in female rats. A dose-response effect study showed that the ED$_{50}$ was 150 mg/kg b.w. Extract doses higher than 100 mg/kg b.w. were more effective than 30 mg/kg of lansoprazol in inhibiting gastric lesions. A methanolic fraction (257.12 mg/kg) which reduced gastric lesion at 88.20% is likely to contain the active principle of the antiulcer effect (Konan, 2007).

2. **Subacute toxicity and genotoxicity assay:** Subacute toxicity and genotoxicity assays were carried out for 30 days. The crude extract did not produce toxic symptoms in rats in doses up to 2000 mg/kg. Based on biochemical analyses of renal and hepato-biliary functions, such as the level of urea, creatinine, transaminases and alkaline phosphatase, the tolerance of extracts in rats was determined and was also confirmed by histopathological exams. Genotoxicity was accessed by the Ames test in *Salmonella typhimurium* strains TA97, TA98, TA100, TA102 and by the bone marrow micronucleus test in mice. The extract was shown to induce frameshift, base pair substitution and damage to the chromosomes (Konan, 2007).

3. **Cytotoxicity of cashew flavonoids towards malignant cell lines:** In a sub-acute toxicity assay it was found that an ethanolic extract of cashew leaves elicited lymphopenia in rats. The extract was also found to be cytotoxic and to induce apoptosis in Jurkat (acute lymphoblastic leukemia) cells. It was also observed that agathisflavone induces apoptosis in Jurkat cells and that this is the likely mechanism of agathisflavone specific cytotoxicity (Konan, 2010).
4. **Vasorelaxation induced in isolated rat aorta and mesenteric vascular bed:** In this study, the vasodilatory actions of nine edible tropical plant extracts were investigated. The vascular effect on the aortic ring preparations were mainly endothelium-dependent, and mediated by nitric oxide (NO) as supported by the inhibition of action in the presence of N[omega]-nitro-l-arginine (NOLA), a nitric oxide synthase (NOS) inhibitor, or by the removal of endothelium (Runnie, 2004).

5. **Antioxidant and nitric oxide inhibition activities:** The antioxidant properties and the effect on nitric oxide (NO) production, in lipopolysaccharide-activated macrophages, of 12 traditional vegetables of the Malaysia were investigated. Antioxidant activity of the hydroalcoholic extracts of cashew leaves and other plants was evaluated by measuring the production of hydroperoxide and its degradation product (malonaldehyde) resulting from linoleic acid oxidation using ferric thiocyanate and thiobarbituric acid methods, respectively. Radical-scavenging potential was also evaluated using the 1,1-diphenyl-2-picrylhydrazyl radical. Griess assay was used to assess NO-inhibitory activity of the extracts (Abas, 2006).

6. **Antibacterial activity:** Crude extracts from eight Nigerian medicinal plants, used traditionally in the treatment of infectious and septic diseases in both humans and animals were screened *in vitro* for antibacterial activity, using the hole-plate diffusion method. Most of the extracts were active against Gram-positive bacteria. Two of the plants, *Angeiossus schimperi* and *Anacardium occidentale*, had good antibacterial activity against *Escherichia coli* and *Pseudomonas aeruginosa* which are Gram-negative bacteria (Kudi, 1999).

7. **In vitro anti-rotavirus activity against diarrhea:** In this work, 12 medicinal plant species were screened for simian (SA-11) and human (HCR3) rotaviruses inhibition in vitro. At non-cytotoxic concentrations, the extract of *Anacardium occidentale* L. (Anacardiaceae) leaves (4 μg/ml) was not effective in inhibiting human and simian rotavirus. Hence, cashew leaves may not be useful in the treatment of human diarrhea if the etiologic agent is a rotavirus (Gonçalves, 2005).
8. **Antidiabetic activity in Streptozotocin-induced adult rat model:** The protective effect of *Anacardium occidentale* aqueous extract against streptozotocin-induced diabetes was evaluated in adult rats. The results showed that the aqueous extract of cashew at doses of 250 and 35.175 mg / kg has a remarkable hypoglycaemic effect in 1hr 30 min after gavage. The maximum hypoglycemic effect (p <0.001) was observed 3 h after treatment of rats with doses of 175 and 250 mg / kg (25% and 24% reduction). The most pronounced effect was observed with a dose of 175 mg / kg which is significantly active (p <0.05) 8h after administration. The administration of this extract (175mg/kg) twice a day significantly reduced (p <0.01) serum glucose levels of 43% in diabetic rats after 3 days of treatment. The lowest dose (35 mg / kg) resulted in a nonsignificant decrease of 4%. Moreover, there is a decrease in glycosuria in diabetic rats treated. The administration of the extract in doses of 175 and 250 mg / kg after the glucose tolerance test resulted in an attenuation of the increase in blood glucose 1 hour after administration. Subsequently, blood glucose decreased in all groups but not significantly in the treated rats. These results indicate a hypoglycemic activity of aqueous extract of leaves of cashew (Kamtchouing, 2001).

9. **Phytochemical investigations of leaves, fruit and bark:** In this study the tender leaves were found to contain ethylgallate, and hyperoside, leucocyanidin and leucodelphinidin. Bark was found to contain condensed tannins. No crystalline components were isolated. Flowers exhibited the presence of ethyl gallate; triacetate, tribenzoate, trimethyl ether, gallic acid, quercetin, hyperoside, and gallic acid (Subramanian, 1969).

10. **Antifungal activity:** The aqueous extract was tested for antifungal activity. The, aqueous extract and the supernatants, precipitates (obtained by ethanol precipitation) were investigated against skin diseases by the Brazilian population. The agar diffusion and broth dilution methods were used to assess the activity against three fungi: *Candida albicans, Trichophyton rubrum* and *Cryptococcus neoformans*. The separation of macromolecules from metabolites, enhanced antifungal activity (Schmourlo, 2004).
11. Biological screening by radioligand-binding techniques: The methanol:chloromethane extract of the bark and leaves of *Anacardium occidentale* L., inhibited the [3H]-AT II binding (angiotensin II AT1 receptor) more than 50%. (Caballero, 2001).

12. Antihyperglycemic and renal protective activity: Rats with streptozotocin (STZ)-induced type 1 diabetes were chronically treated with hexane extract of *Anacardium occidentale* (AO). The functional and histological alterations of kidneys were studied. Albino rats were divided into 7 groups (n = 5) receiving graded doses of hexane extract of *Anacardium occidentale* leaf by gavage, (150 and 300 mg/kg/day) and insulin (5 IU/kg). AO at the dose of 300 mg/kg/day, showed significant reduction (P < 0.05) of blood glucose level, total protein excreted, glycosuria and urea in diabetic rats. *Anacardium* treatment, initiated 3 days after diabetes induction, reduced destruction of renal structure and other metabolic disturbances more than when treatment was initiated two weeks after. Histopathological study showed that *A. occidentale* significantly reduced accumulation of mucopolysaccharides in the kidneys of diabetic animals. The extract of AO at the dose of 300 mg/kg had no nephrotoxic potential in normal rats. The present study demonstrates the efficacy of *Anacardium occidentale* (hexane extract) in reducing diabetes-induced functional and histological alterations in the kidneys (Tedong, 2006).

13. Effects of leaf extract on reproductive disorders in streptozotocin-induced diabetic rats: Effects of *A. occidentale* leaf extract on reproductive disorders were evaluated in streptozotocin-induced diabetic male rats. Hexane extract of *A. occidentale* at doses of 150 and 300 mg/kg/day administered to diabetic rats caused a 25% and 74.6% reduction respectively in glycaemia after 5 weeks of treatment. This effective dose also caused a significant (p > 0.05) increase in testicular protein levels, a noticeable decrease in vesicular fructose levels by 47%, improved epididymal function reflected in an overexpression of a-glucosidase activity, an increase in the number of spermatozoa by 108.4% and an increased fertility rate by 66%; and an improvement in testicular tissue. The beneficial effect of *A. occidentale* extract on blood glucose levels and reproductive function could be explained by the presence of polyphenols and alkaloids (Tedong, 2007).
14. Hypoglycemic Effect of Methanol Extract on Streptozotocin-induced Diabetic Rats: The effect of the methanol leaf extract, dichloromethane, ethyl acetate and n-hexane fractions from *Anacardium occidentale* Linn. was investigated in streptozotocin-induced diabetic rats. Oral administration of methanol extract at doses of 35, 175 and 250 mg/kg significantly reduced blood glucose levels in diabetic rats 3 hours after administration. Of three different doses, maximum reduction of 37 and 35% in blood glucose levels was respectively observed with doses of 175 and 250 mg/kg. When administered repeatedly, the blood glucose reducing effect of the methanol extract at the dose of 175 mg/kg in diabetic rats became more pronounced (48%). Fractions from the methanol extract at the dose of 175 mg/kg also decreased the blood glucose levels in diabetic rats after repeated administration. The n-hexane fraction produced the maximum hypoglycemic effect (45%) and the same dose of the dichloromethane and ethyl acetate fractions respectively reduced hyperglycemia by 21 and 41% at the end of the treatment. On the other hand, a significant decrease in urine glucose levels was observed in diabetic rats after repeated administration of the methanol extract and fractions. These results suggest the hypoglycemic effect of the methanol extract of *A. occidentale* in streptozotocin-induced diabetic rats (Sokeng, 2007).
4.2 SCIENTIFIC REPORTS PUBLISHED FOR CASHEW TESTA

1. **Free radical scavenging activity:** Antioxidant activity of ethanolic extract of Cashew nut (*Anacardium occidentale* L.) skin was evaluated by employing various *in vitro* antioxidant assay systems. The cashew nut skin extract (CSE) demonstrated promising antioxidant activity in 2,2'-azino-bis (3-ethylbenzthiazoline-6-sulphonic acid) (ABTS) radical scavenging assay, superoxide scavenging assay, and deoxyribose oxidation assay (Kamath, 2007).

2. **Biochemical perturbations in rat pancreas and its attenuation by cashew nut skin extract:** The extent of protection offered by cashew nut skin extract (CSE) against the damage induced in rat pancreas by sub chronic doses dimethoate, an organophosphorous pesticide was studied. DM treated rats exhibited impaired glucose tolerance at the end of two months as indicated by Oral glucose tolerance test (OGTT), while DM treated rats with CSE supplements showed normal glucose tolerance. Treatment with CSE significantly protected rat pancreas from injury, thus ameliorating and restoring tissue antioxidant status and also conferring normal glucose tolerance (Kamath, 2008).

3. **Polyphenols of cashew kernel testa:** The chemical nature of the polyphenols of cashew kernel testa has been determined by means of 2-dimensional paper chromatography. Presence of (+) catechin and (-) epicatechin as the major polyphenols has been confirmed by co-chromatography with authentic samples. Proanthocyanidins have been studied by treatment with hot acid and identification of the resultant anthocyanidins. Leucocyanidins and leucopelargonidins have been noticed as monomeric components, whereas polymeric proanthocyanidins contain in addition small quantities of leucodelphinidin. Individual components have been quantitatively estimated colorimetrically with Folin-Denis reagent, after separation by fractional extraction using solvents of increasing polarity and paper chromatography. The characteristic bluish-black discoloration noticed in cashew-nuts has been identified as an iron-polyphenol complex formed during processing. The polyphenols were found to be derived from the testa (Mathew, 1970).
4. **Studies on oleoresinous varnishes and their natural precursors:** Condensed tannins extracted from the seed testa of *Anacardium occidentale* is subjected to phytochemical and spectral studies such as UV and 13C NMR. Shell of *Cocos nucifera* on treatment with acid yields acid hydroxylates containing furfural which when condensed with tannins of *A. occidentale* form phenol–formaldehyde type resins. The spectral and physico-chemical properties of the resins are studied. Varnishes are prepared from these resins using linseed oil/linseed oil–tung oil. The service performances of the varnishes including their impedance spectra were evaluated. The results show that varnishes with good gloss and chemical resistivity can be prepared from these waste materials (Kumar, 2004).

5. **Plant regeneration through direct somatic embryogenesis:** A protocol of plant regeneration through direct somatic embryogenesis was established for the first time on cashew using seed coat explants. Embryos exhibited all stages of development, i.e. from globular to cotyledonary. Fifty percent of the embryos underwent conversion upon transfer to MS medium containing 4.65 mM kinetin and plantlets were successfully transferred to field conditions. Ninety percent survived in field conditions (Martin, 2003).
4.3 SCIENTIFIC REPORTS PUBLISHED FOR STEM BARK OF CASHEW

1. **Genotoxicity and antigenotoxicity activity:** The genotoxic and protective activities of cashew stem bark methanolic extract, *in vitro* was studied. Methyl methanesulfonate (MMS) was used as a positive control, to compare possible mechanisms of DNA damage induction in the Comet assay (Barcelos, 2007).

2. **Gum exudates of cashew tree:** Gum exudates from the Brazilian cashew-nut tree (*Anacardium occidentale* L.) contained traces of the reducing sugars, rhamnose (0.005%), arabinose (0.03%), mannose (0.007%), galactose (0.03%), glucose (0.02%), (0.05%), (0.008%) and (0.008%). The structure of this polysaccharide was determined and found to differ from the reports previously published for the gum of a tree growing in India, lacking units of 4-O-methylglucuronic acid (Menestrina, 1998).

3. **Study on properties of Gum:** The composition and solution properties of Indian and Papuan specimens of the gum from *Anacardium occidentale* have been studied and found to be closely similar. Contrary to earlier reports by Indian workers, this gum does not contain galacturonic acid. It does, however, contain glucose; this appears to be the first report of the presence of this sugar in a plant gum exudates (Douglas, 1974).

4. **Mutagenicity and antimutagenicity of cashew stem bark:** The mutagenicity and antimutagenicity of cashew stem bark methanolic extract (CSBME) on cell cultures of Chinese hamster lung fibroblasts (V79) was assessed. The data obtained in the chromosome aberrations (CA) test showed a significant reduction in CA frequency in the cultures treated with DXR and extract in comparison with those that received only DXR during the cell cycle phases G1 and S and throughout the entire cycle, as well as the absence of mutagenicity in all the treatments realized (Gustavo, 2007).

5. **Enzymatic and inhibitory activities of cashew tree gum exudates:** The gum exudate from the *Anacardium occidentale* tree has been analysed for carbohydrate, Kjeldahl nitrogen, protein and phenols, and for the activities of

6. Structural analysis of the gum polysaccharide from *Anacardium occidentale*: The gum exudate from *Anacardium occidentale* contains galactose (61%), arabinose (14%), rhamnose (7%), glucose (8%) and glucuronic acid (5%) in addition to small amounts (<2%) of each of mannose, xylose and 4-O-methylglucuronic acid. Sequential Smith-degradations of *Anacardium occidentale* gum, and methylation analyses of the gum and of its degradation products indicated a highly-branched galactan framework consisting of chains of [beta]-(1-3)-linked D-galactose residues branched and interspersed with [beta]-(1-6) linkages (Anderson, 1975).

7. Anti-inflammatory actions of tannins isolated from the bark of *Anacardium occidentale* L.: A mixture of tannins (hydrolysable and non-hydrolysable) obtained from the bark of *Anacardium occidentale* L., on i.p. injection, demonstrated apparent anti-inflammatory activity in carrageenan- and dextran-induced rat paw oedemas, cotton pellet granuloma test and adjuvant-induced polyarthritis in rats. The tannins i.p. also inhibited acetic acid-induced 'writhing responses' in mice and were found to antagonise the permeability-increasing effects in rats of certain mediators of inflammation and to inhibit the migration of leucocytes to an inflammatory site (Mota, 1985).

8. Sub-chronic Hepatotoxicity: The phytochemical compositions and acute toxicity of the extract were determined. Toxicity profiles of the extract on some liver function parameters were evaluated following a sub-chronic oral administration at doses of 1.44 and 2.87 g/kg. The sub-chronic administrations of *Anacardium occidentale* inner stem bark extract did not significantly (p< 0.05) depress the function of hepatocytes in Wistar rats. The (+)-cyanidanol-3 (made as CATERGEN, supplied by Zyma-Biogal Pharmaceutical Works, Debrecen, Hungary,) was is used as an antihepatotoxic and hepatoprotective drug in both men and animals against alcoholic and experimental liver injury. Ethanol was administered ad lib to CFY rats to cause mild alcoholic liver damage together with 200 mg/kg/day (+)-cyanidanol-3 to
prevent the tissue. The (+)-cyanidanol-3 prevents changes and the morphometric parameters in the treated group were almost the same as in the controls. The treatment with (+)-cyanidanol-3 alone does not affect the hepatic tissue parameters. The results show the hepatoprotective effect of (+)-cyanidanol-3 and the suitability of the morphometric method for quantitative comparison of normal and experimentally-altered liver cells. (Varga, 1989; Ryle 1981; and Ryle 1983).

9. **Stimulation of glucose uptake in C2C12 muscle cells by cashew extracts:** The anti-diabetic properties of cashew plant parts were studied using differentiated C2C12 myoblasts (myotubes) and rat liver mitochondria. Hydroethanolic extract of cashew seed (CSE) and its active component, anacardic acid (AA), stimulated glucose transport into C2C12 myotubes in a concentration-dependent manner. Extracts of other parts (leaves, bark and apple) of cashew plant were inactive (Tedong, 2010).

10. **Effects on in vivo inflammatory models:** The methanol extract of *Anacardium occidentale* stem bark was evaluated for activities against the lipopolysaccharide (LPS)-induced septic shock, as well as LPS-induced microvascular permeability in mice. Pre-treatment with *Anacardium occidentale* extract (25-200 mg/kg) caused a dose-dependent and significant (p <0.05) reduction in the elevated levels of alanine and aspartate aminotransferases in the sera of D-galactosamine-primed mice injected with LPS. A dose-related inhibition of LPS-induced microvascular permeability in mice was also produced by pentoxifylline, and the extract (Olajide, 2004).

11. **Hypoglycaemic effect of stigmast-4-en-3-one and its corresponding alcohol:** Intravenous administration of the hexane extract of the bark of *Anacardium occidentale* (cashew) in normal, healthy dogs produced a significant lowering of the blood glucose levels. Pursuit of the hypoglycaemic principle(s) in the hexane extract resulted in the isolation and characterization of two compounds, stigmast-4-en-3-ol and stigmast-4-en-3-one (Alexander, 2004).
4.4 SCIENTIFIC REPORTS PUBLISHED FOR ROOTS OF CASHEW

1. Hypoglycemic potencies of crude ethanolic extracts of cashew roots: The crude ethanolic extract of cashew root and pawpaw fruits showed hypoglycemic potencies, however, the crude ethanolic extract of cashew roots showed more hypoglycemic potency than the crude extract of pawpaw fruits in both guinea pigs and rats. The work concludes that ethanolic extract of cashew root and pawpaw fruit contains natural substances that can be harnessed for the treatment and management of diabetes mellitus (Egwim, 2005).

4.5 SCIENTIFIC REPORTS PUBLISHED FOR CASHEW NUT SHELL OIL

1. Gastroprotection activity: The gastroprotection effect of anacardic acids against the ethanol-induced gastric damage was studied to examine the underlying mechanism(s). Gastroprotection was assessed in relation to inhibition of gastric lesion area. These results suggest that anacardic acids afford gastroprotection principally through an antioxidant mechanism, activation of capsaicin-sensitive gastric afferents, stimulation of endogenous prostaglandins and nitric oxide, and opening of K+ATP channels (Talita, 2010).

2. Supercritical fluid extraction of cashew nut shell liquid: Nut shell liquid can be separated from fragmented honeycombed cashew shell material without employing thermal techniques with a pressure profile method that uses supercritical carbon dioxide as solvent. Using the method, extraction yields of cashew nut shell liquid (CNSL) of up to 10 times than those obtained by usual supercritical fluid extraction were achieved. Analysis with liquid chromatography of the extracts contained approximately 50 mol% anacardic acids, 29 mol% cardols, and 21 mol% cardanols including mono-, di-, and tri-ene constituents (Setianto, 2009).

3. Phenolic constituents of natural cashew nut-shell liquid: The phenolic constituents of natural cashew nut-shell liquid (CNSL) from *Anacardium occidentale* have been separated by high-performance liquid chromatography by the reversed-phase method. The relative molar response values for the saturated
component phenols have been determined and the use of an internal standard has led to a quantitative procedure (Tyman, 1984).

4. **Cashew nut allergy**: It is the second most commonly reported tree nut allergy in the United States. The cloned allergen, designated Ana o 3, was identified as 2S albumin. MALDI-TOF mass spectroscopy of native Ana o 3 yielded a molecular mass of 12,598 d. This 2S albumin protein is a major allergen in cashew nut and demonstrates a possible basis for cross-reactivity with walnut 2S albumin (Jason, 2005).

5. **Compositional studies on nut shell oil**: An extensive gas chromatographic investigation of alternative stationary phases to polyethyleneglycol adipate which are suitable for the quantitative analysis of hydrogenated and methylated natural and technical cashew nut-shell liquid. A comparison has been drawn between the ionisation processes in the flame ionisation detector and in mass spectrometry (Tyman, 1977).

6. **Spectroscopic and chromatographic analysis**: Natural cashew nut-shell liquid has been analysed by thin-layer chromatography (TLC) combined with spectrophotometry. In a direct method the bands were examined in situ by an adsorbance method involving a 'flying spot' scanning procedure and densitometry (Tyman, 1978).

7. **Gas—liquid chromatography analysis of nut shell oil**: Cashew nut-shell liquid (CNSL) of natural origin or as the technical product obtained by industrial decarboxylation, has been analysed by gas—liquid chromatography (Tyman, 1976).

8. **Supercritical extraction of nut shell oil**: The separation of CNSL from the pericarp of the cashew nut with supercritical carbon dioxide was carried out. The pressure profile extraction method proposed in this work increases the possible CNSL extraction yields and greatly reduces the amount of CO2 required for CNSL separation (Smith, 2003).
9. **Crosslinked materials from cashew gum:** Cashew gum (CG) and carboxymethylated CG (CMCG) were synthesized using epichlorohydrin (E) as the crosslinking agent. The products were characterized by 13C nuclear magnetic resonance, IR spectroscopy, swelling degree and thermal analysis (Durcilene, 2006).

10. **Degradation products of carotenoid degradation:** The influence of organic acid and heating treatments on carotenoid degradation on a simulated cashew apple juice was assessed by high performance liquid chromatography coupled with a photodiode array and mass spectrometry detectors. The facts indicated that isomerisation and oxidation to both coloured and non-coloured compounds were the main reactions occurring during heating of carotenoids in aqueous-based and juice systems (Leila, 2009).

11. **Phenolic lipid composition during development of cashew:** Quantitative composition of the major phenolic lipids (anacardic acids, cardols and cardanols) of the apple, kernel and shell of the cashew plant have been determined at various stages of development by high-performance liquid chromatography (Shobha, 1992).

12. **Quantitative analysis of the phenolic lipids:** The novel separation of the constituent phenols in technical cashew nut-shell liquid from the industrial processing of *Anacardium occidentale* has been effected by high-performance liquid chromatography. Gradient elution with tetrahydrofuran and acetonitrile has also enabled the polymeric material to be estimated in the various types of technical cashew nut-shell liquid examined (Tyman, 1981).

13. **Promoting action of cashew nut shell oil mouse skin tumour model:** The commercially available oil derived from the shell of cashew nut (*Anacardium occidentale*) was tested for its potency in promoting the DMBA-initiated cells into papillomas in a murine two-stage skin tumorigenesis model system. Few speculative mechanisms for the observed effect of cashew nut shell oil on initiated skin are discussed (Banerjee, 1992).
14. Antioxidant properties and chemical composition of technical cashew nut shell liquid (tCNSL): The antioxidant activity of the technical cashew nut shell Liquid (tCNSL) using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging assay and the xanthine oxidase assay, as well as in vivo evaluation by Saccharomyces cerevisiae assay. Also, the chemical composition of tCNSL was determined by gas chromatography-mass spectrometry (GC-MS) (Teresinha, 2011).
4.6 SCIENTIFIC REPORTS PUBLISHED FOR CASHEW SHOOTS

1. **Free Radical scavenging activity of cashew shoots:** The total phenolic content and antioxidant activities of methanol, hexane and ethyl acetate extracts of the shoots of *Anacardium occidentale* were measured. Total phenolic content was assessed by the Folin-Ciocalteau assay whereas antioxidant activities were assessed by measuring the ability of the extracts to scavenge the ABTS$^+$ and DPPH$^-$ radicals, superoxide anion radicals and nitric oxide radicals as well as their ability to reduce ferric ions. The order of the antioxidant potency of the plant extract is methanol > ethyl acetate > hexane. The methanol extract contained more than 7 fold of total phenolic content compared to the hexane and ethyl acetate extracts indicating the likely possibility that the observed antioxidant activities were partly contributed by the phenolics (Nurhanani, 2008).

2. **In vitro adventitious shoot formation from cotyledon explants of cashew:** Excised cotyledons from mature embryos of cashew (*Anacardium occidentale* L.) developed adventitious shoots from the proximal end when cultured on Murashige and Skoog's (MS) medium. About 55% of in vitro raised shoots developed roots. This procedure was first applicable to the three commercial high-yielding cultivars of cashew (Ananthakrishnan, 2002).
4.7 SCIENTIFIC REPORTS PUBLISHED FOR CASHEW APPLE

1. Determination of Flavonoids: Liquid chromatography, with diode array detection and electrospray ionization mass spectrometry (LC-DAD-ESI/MS), was used to identify and quantify flavonoids in cashew apple. One anthocyanin and thirteen glycosylated flavonols were detected in a methanol-water extract. (Sousa, 2007).

2. Characterisation of residues in peduncle bagasse: The characterization of the incineration ashes of the primary residue derived from the cashew's juice extraction, the peduncle bagasse. Measurements showed that these ashes represent only 3% of the incinerated material. EDX analysis indicated the presence of the following elements: C, O, P, K, Mg, S, Na, Al and Si. X-ray diffraction and thermal analyses pointed KHCO$_3$ (54.17%), K$_2$SO$_4$ (34.08%) and MgKPO$_4$.6H$_2$O (10.06%) as the most significant crystalline phases (Ricardo, 2007).

3. Determination of constituents of skin and flesh of cashew apple: Monomeric phenols were extracted by acetone/water (60:40) from the skin and flesh of four cashew apple genotypes from Brazil and Benin (West Africa), purified by absorption chromatography and subjected to HPLC-DAD/ESI-MS analysis. Skins were found much richer than fleshes in simple phenolics (Laetitia, 2009).

4. Determination of volatile components in cashew apple: An essence of fresh cashew ‘apple’, was analysed by GC and by GC/MS using both EI and CI techniques. The fruit produced a very small quantity of aroma volatiles (ca 3.6 [µg/kg fresh fruit), much less than that obtained from most similar tropical fruits. Five aldehydes comprised ca 26% of the sample, but terpene hydrocarbons (38%) provided the major group of compounds (Alexander, 1982).

5. Carotenoids and ascorbic acid from cashew apple: The levels of carotenoids were analysed in red and yellow cashews from the Southeast and Northeast, respectively. The total carotenoid levels of the rounded red fruits were 1.5 and 1.7 times lower than those found in the yellow and red varieties, respectively, all being from the Northeast region. Yellow fruits from the Northeast presented 1.7
times higher provitamin A levels than those from the Southeast whereas, for the red variety, the values were similar (Raquel, 2003).

6. **Essential oils of the leaves, fruits, and flowers cashew**: Essential oils of various parts of yellow and red variety of (*Anacardium occidentale* L.) were obtained by hydrodistillation and analysed by GC/MS. The oil of the leaves from red cashew was dominated by (E)-[beta]-ocimene (28.8%), [alpha]-copaene (13.6%), and[delta]-cadinene (9.1%). The major constituents of the oil from fruits of the red variety were palmitic (19.6%) and oleic (19.6%) acids, while palmitic acid (11.4%), furfural (10.0%), 4-hydroxydodecanoic acid lactone (8.2%), (E)-hex-2-enal (7.2%), (Z)-hex-3-enol (6.2%), and hexadecanol (6.2%) were the principal components identified in the oil of yellow cashew. The main constituents found in the oil of the flowers of red cashew were [beta] -caryophyllene (26.0%), methyl salicylate (12.8%), and benzyl tiglate (11.3%) (Jose, 2000).

7. **Antioxidant capacity of cashew apple**: The content of anacardic acids, cardanols and cardols in cashew apple, nut (raw and roasted) and cashew nut shell liquid (CNSL) were analysed. A mixture of anacardic acids (10.0 mg/ml) showed the higher antioxidant capacity (*IC*₅₀ = 0.60 mM) compared to cardols and cardanols (*IC*₅₀ > 4.0 mM). The antioxidant capacity of anacardic acid-1 is more related to inhibition of superoxide generation (*IC*₅₀ = 0.04 mM) and xanthine oxidase (*IC*₅₀ = 0.30 mM) than to scavenging of hydroxyl radicals (Trevisan, 2006).

8. **Antioxidant activity of anacardic acids**: Anacardic acids, 6-pentadec(en)ylsalicylic acids isolated from the cashew *Anacardium occidentale* L. (Anacardiaceae) nut and apple, were found to possess preventive antioxidant activity while salicylic acid did not show this activity. Anacardic acids act as antioxidants in a variety ways, including inhibition of various prooxidant enzymes involved in the production of the reactive oxygen species and chelate divalent metal ions such as Fe²⁺ or Cu²⁺, but do not quench reactive oxygen species. The C15-alkenyl side chain is largely associated with the activity (Kubo, 2006).

9. **Design and evaluation of anacardic acid derivatives as anticavity agents**: On the basis of antibacterial effect of anacardic acids, 6-pentadecenylsalicylic acids,
isolated from the cashew apple, *Anacardium occidentale* L. (Anacardiaceae), a series of 6-alk(en)ylsalicylic acids were synthesized and tested for their antibacterial activity against *Streptococcus mutans* ATCC 25175. Among them, 6-(4',8'-dimethylnonyl)salicylic acid was found to exhibit the most potent antibacterial activity against this cariogenic bacterium with the minimum inhibition concentration (MIC) of 0.78 µg/ml (Green, 2008).

10. **Cell proliferation inhibitory and apoptosis-inducing properties of anacardic acid in human breast cancer MDA-MB-231 cells:** Anacardic acid and lunasin are two plant-derived compounds that show inhibitory effects on cell proliferation and inducing properties of apoptosis in human breast cancer MDA-MB-231 cell line. Both lunasin and anacardic acid exert their effects through the modulation of expression of several genes involved in cell cycle, apoptosis and signal transduction. The results introduce these two compounds as a promising strategy to prevent/treat breast cancer (Hsieh, 2011).

11. **Characterization of anacardic acids by micellar electrokinetic chromatography and mass spectrometry:** Capillary electrophoresis for separation of anacardic acids (6-alkylsalicylic acids) has been studied. Separation of anacardic acids were achieved in the polydimethylacrylamide-coated capillary using 10 mM phosphate background electrolyte pH 6.5 with addition of 1 M urea, 20% acetonitrile, 10 mM of [beta]-cyclodextrin and 1 mM of heptakis-6-sulfo-[beta]-cyclodextrin. Mass spectrometry was used for the identification of anacardic acids in the extract from cashew nuts in single and tandem mode using Q-TOF instrument (Cesla, 2006).

12. **Flavonols in fresh and processed fruits:** Flavonols (myricetin, quercetin and kaempferol) and flavones (luteolin and apigenin) were determined in Brazilian fruits, using a previously optimized and validated HPLC method. The best sources of flavonols among the fruits investigated were pitanga, cashew-apple, acerola and apple, the first three being analyzed for the first time (Ribani, 2009).

13. **Study on antioxidant activity of dry fruits:** The antioxidant activity of cashew nut through several chemical and biochemical assays: reducing power, lipid
peroxidation damage in biomembranes, determination of antioxidant enzymes activity (SOD and CAT) was carried out. The higher phenolic content was found in walnuts followed by almonds cashew nut, chironji and least phenolic content was found in raisins (Mishra, 2010).

14. Glycaemic effects in normal and streptozotocin diabetic mice: The traditional treatment of diabetes mellitus in northern Europe was studied using normal and streptozotocin diabetic mice to evaluate effects on glucose homeostasis. Cashew leaves were administered in the diet (6.25% by weight) and/or as decoctions or infusions in place of drinking water, to coincide with the traditional method of preparation. Treatment was given for 28 days. After administration of streptozotocin (200 mg/kg) cashew, did not significantly affect the parameters of glucose homeostasis studied (basal glucose and insulin, insulin-induced hypoglycaemia, glycated haemoglobin and pancreatic insulin concentration). (Swanston, 1989).
4.8 SCIENTIFIC REPORTS PUBLISHED FOR FLOWERS OF CASHEW

**Pollen allergy in patients with asthma:** Upon exposure to cashew pollen the patients in study, (40%) had positive skin test reactions in various grades. About 90.9% patients had a positive bronchial provocation tests (BPT) result, and the majority of patients had grade III and grade IV reactions. This study provided us with knowledge of an additional pollen, *Anacardium occidentale*, which could trigger an asthmatic response in allergic individuals (Fernandes, 1995).

4.9 PATENTS PUBLISHED FOR CASHEW, CATECHIN, AND CYANIDANOL

- A United States patent is also published regarding the process of coating cashew nut with intact testa in order to make it edible. As a part of the processing of cashew nuts a process was designed to coat the cashews (with testa) with flavours, spices, honey and sugar infusions (Harikrishnan, 2005).

- A patent to control the isomerisation of (-)-epicatechin and (+) – catechin and their altered monomers in edible products was published. The process involves use of open food processor under reduced oxygen pressure or a closed vessel (Hammerstone, 2007, 2010).

- A United States patent related to pharmaceutical preparations containing (+)-cyanidanol-3-ol derivates, particularly suitable for treating liver and venous diseases at the dose range between 10-500 mg/kg in rats is reported (Ballenegger, 1987).
This review summarizes the literature on different pharmacological effects, phytochemical analysis and various other applications of *Anacardium occidentale* L. (Cashew). *Anacardium occidentale* is a medicinal plant reputed in folk lore system of medicine in tropical countries, and of which the pharmacological activities have been scientifically demonstrated. The review of literature reflects the plant parts involved, the nature of the extracts used and the names of the active principles.

### 4.1 SCIENTIFIC REPORTS PUBLISHED FOR LEAVES OF CASHEW

1. **Antiulcerogenic activity:** The antiulcerogenic effect of a hydroethanolic extract of *Anacardium occidentale* L. leaves was investigated. The extract inhibited gastric lesions induced by HCl/ethanol in female rats. A dose-response effect study showed that the ED$_{50}$ was 150 mg/kg b.w. Extract doses higher than 100 mg/kg b.w. were more effective than 30 mg/kg of lansoprazol in inhibiting gastric lesions. A methanolic fraction (257.12 mg/kg) which reduced gastric lesion at 88.20% is likely to contain the active principle of the antiulcer effect (Konan, 2007).

2. **Subacute toxicity and genotoxicity assay:** Subacute toxicity and genotoxicity assays were carried out for 30 days. The crude extract did not produce toxic symptoms in rats in doses up to 2000 mg/kg. Based on biochemical analyses of renal and hepato-biliary functions, such as the level of urea, creatinine, transaminases and alkaline phosphatase, the tolerance of extracts in rats was determined and was also confirmed by histopathological exams. Genotoxicity was accessed by the Ames test in *Salmonella typhimurium* strains TA97, TA98, TA100, TA102 and by the bone marrow micronucleus test in mice. The extract was shown to induce frameshift, base pair substitution and damage to the chromosomes (Konan, 2007).

3. **Cytotoxicity of cashew flavonoids towards malignant cell lines:** In a sub-acute toxicity assay it was found that an ethanolic extract of cashew leaves elicited lymphopenia in rats. The extract was also found to be cytotoxic and to induce apoptosis in Jurkat (acute lymphoblastic leukemia) cells. It was also observed that agathisflavone induces apoptosis in Jurkat cells and that this is the likely mechanism of agathisflavone specific cytotoxicity (Konan, 2010).
4. Vasorelaxation induced in isolated rat aorta and mesenteric vascular bed: In this study, the vasodilatory actions of nine edible tropical plant extracts were investigated. The vascular effect on the aortic ring preparations were mainly endothelium-dependent, and mediated by nitric oxide (NO) as supported by the inhibition of action in the presence of $\text{N} \omega \text{-nitro-l-arginine (NOLA)}$, a nitric oxide synthase (NOS) inhibitor, or by the removal of endothelium (Runnie, 2004).

5. Antioxidant and nitric oxide inhibition activities: The antioxidant properties and the effect on nitric oxide (NO) production, in lipopolysaccharide-activated macrophages, of 12 traditional vegetables of the Malaysia were investigated. Antioxidant activity of the hydroalcoholic extracts of cashew leaves and other plants was evaluated by measuring the production of hydroperoxide and its degradation product (malonaldehyde) resulting from linoleic acid oxidation using ferric thiocyanate and thiobarbituric acid methods, respectively. Radical-scavenging potential was also evaluated using the 1,1-diphenyl-2-picrylhydrazyl radical. Griess assay was used to assess NO-inhibitory activity of the extracts (Abas, 2006).

6. Antibacterial activity: Crude extracts from eight Nigerian medicinal plants, used traditionally in the treatment of infectious and septic diseases in both humans and animals were screened in vitro for antibacterial activity, using the hole-plate diffusion method. Most of the extracts were active against Gram-positive bacteria. Two of the plants, Angeiossus schimperi and Anacardium occidentale, had good antibacterial activity against Escherichia coli and Pseudomonas aeruginosa which are Gram-negative bacteria (Kudi, 1999).

7. In vitro anti-rotavirus activity against diarrhea: In this work, 12 medicinal plant species were screened for simian (SA-11) and human (HCR3) rotaviruses inhibition in vitro. At non-cytotoxic concentrations, the extract of Anacardium occidentale L. (Anacardiaceae) leaves (4 $\mu$g/ml) was not effective in inhibiting human and simian rotavirus. Hence, cashew leaves may not be useful in the treatment of human diarrhea if the etiologic agent is a rotavirus (Gonçalves, 2005).
8. **Antidiabetic activity in Streptozotocin-induced adult rat model:** The protective effect of *Anacardium occidentale* aqueous extract against streptozotocin-induced diabetes was evaluated in adult rats. The results showed that the aqueous extract of cashew at doses of 250 and 35.175 mg / kg has a remarkable hypoglycaemic effect in 1hr 30 min after gavage. The maximum hypoglycemic effect (p <0.001) was observed 3 h after treatment of rats with doses of 175 and 250 mg / kg (25% and 24% reduction). The most pronounced effect was observed with a dose of 175 mg / kg which is significantly active (p <0.05) 8h after administration. The administration of this extract (175mg/kg) twice a day significantly reduced (p <0.01) serum glucose levels of 43% in diabetic rats after 3 days of treatment. The lowest dose (35 mg / kg) resulted in a nonsignificant decrease of 4%. Moreover, there is a decrease in glycosuria in diabetic rats treated. The administration of the extract in doses of 175 and 250 mg / kg after the glucose tolerance test resulted in an attenuation of the increase in blood glucose 1 hour after administration. Subsequently, blood glucose decreased in all groups but not significantly in the treated rats. These results indicate a hypoglycemic activity of aqueous extract of leaves of cashew (Kamtchouing, 2001).

9. **Phytochemical investigations of leaves, fruit and bark:** In this study the tender leaves were found to contain ethylgallate, and hyperoside, leucocyanidin and leucodelphinidin. Bark was found to contain condensed tannins. No crystalline components were isolated. Flowers exhibited the presence of ethyl gallate; triacetate, tribenzoate, trimethyl ether, gallic acid, quercetin, hyperoside, and gallic acid (Subramanian, 1969).

10. **Antifungal activity:** The aqueous extract was tested for antifungal activity. The, aqueous extract and the supernatants, precipitates (obtained by ethanol precipitation) were investigated against skin diseases by the Brazilian population. The agar diffusion and broth dilution methods were used to assess the activity against three fungi: *Candida albicans, Trichophyton rubrum* and *Cryptococcus neoformans*. The separation of macromolecules from metabolites, enhanced antifungal activity (Schmourlo, 2004).
11. Biological screening by radioligand-binding techniques: The methanol:chloromethane extract of the bark and leaves of *Anacardium occidentale* L., inhibited the [3H]-AT II binding (angiotensin II AT1 receptor) more than 50%. (Caballero, 2001).

12. Antihyperglycemic and renal protective activity: Rats with streptozotocin (STZ)-induced type 1 diabetes were chronically treated with hexane extract of *Anacardium occidentale* (AO). The functional and histological alterations of kidneys were studied. Albino rats were divided into 7 groups (n = 5) receiving graded doses of hexane extract of *Anacardium occidentale* leaf by gavage, (150 and 300 mg/kg/day) and insulin (5 IU/kg). AO at the dose of 300 mg/kg/day, showed significant reduction (P < 0.05) of blood glucose level, total protein excreted, glycosuria and urea in diabetic rats. *Anacardium* treatment, initiated 3 days after diabetes induction, reduced destruction of renal structure and other metabolic disturbances more than when treatment was initiated two weeks after. Histopathological study showed that *A. occidentale* significantly reduced accumulation of mucopolysaccharides in the kidneys of diabetic animals. The extract of AO at the dose of 300 mg/kg had no nephrotoxic potential in normal rats. The present study demonstrates the efficacy of *Anacardium occidentale* (hexane extract) in reducing diabetes-induced functional and histological alterations in the kidneys (Tedong, 2006).

13. Effects of leaf extract on reproductive disorders in streptozotocin-induced diabetic rats: Effects of *A. occidentale* leaf extract on reproductive disorders were evaluated in streptozotocin-induced diabetic male rats. Hexane extract of *A. occidentale* at doses of 150 and 300 mg/kg/day administered to diabetic rats caused a 25% and 74.6% reduction respectively in glycaemia after 5 weeks of treatment. This effective dose also caused a significant (p > 0.05) increase in testicular protein levels, a noticeable decrease in vesicular fructose levels by 47%, improved epididymal function reflected in an overexpression of a-glucosidase activity, an increase in the number of spermatozoa by 108.4% and an increased fertility rate by 66%; and an improvement in testicular tissue. The beneficial effect of *A. occidentale* extract on blood glucose levels and reproductive function could be explained by the presence of polyphenols and alkaloids (Tedong, 2007).
14. Hypoglycemic Effect of Methanol Extract on Streptozotocin-induced Diabetic Rats: The effect of the methanol leaf extract, dichloromethane, ethyl acetate and $n$-hexane fractions from *Anacardium occidentale* Linn. was investigated in streptozotocin-induced diabetic rats. Oral administration of methanol extract at doses of 35, 175 and 250 mg/kg significantly reduced blood glucose levels in diabetic rats 3 hours after administration. Of three different doses, maximum reduction of 37 and 35% in blood glucose levels was respectively observed with doses of 175 and 250 mg/kg. When administered repeatedly, the blood glucose reducing effect of the methanol extract at the dose of 175 mg/kg in diabetic rats became more pronounced (48%). Fractions from the methanol extract at the dose of 175 mg/kg also decreased the blood glucose levels in diabetic rats after repeated administration. The $n$-hexane fraction produced the maximum hypoglycemic effect (45%) and the same dose of the dichloromethane and ethyl acetate fractions respectively reduced hyperglycemia by 21 and 41% at the end of the treatment. On the other hand, a significant decrease in urine glucose levels was observed in diabetic rats after repeated administration of the methanol extract and fractions. These results suggest the hypoglycemic effect of the methanol extract of *A. occidentale* in streptozotocin-induced diabetic rats (Sokeng, 2007).
4.2 SCIENTIFIC REPORTS PUBLISHED FOR CASHEW TESTA

1. **Free radical scavenging activity:** Antioxidant activity of ethanolic extract of Cashew nut (*Anacardium occidentale* L.) skin was evaluated by employing various *in vitro* antioxidant assay systems. The cashew nut skin extract (CSE) demonstrated promising antioxidant activity in 2,2′-azino-bis (3-ethylbenzthiazoline-6-sulphonic acid) (ABTS) radical scavenging assay, superoxide scavenging assay, and deoxyribose oxidation assay (Kamath, 2007).

2. **Biochemical perturbations in rat pancreas and its attenuation by cashew nut skin extract:** The extent of protection offered by cashew nut skin extract (CSE) against the damage induced in rat pancreas by sub chronic doses dimethoate, an organophosphorous pesticide was studied. DM treated rats exhibited impaired glucose tolerance at the end of two months as indicated by Oral glucose tolerance test (OGTT), while DM treated rats with CSE supplements showed normal glucose tolerance. Treatment with CSE significantly protected rat pancreas from injury, thus ameliorating and restoring tissue antioxidant status and also conferring normal glucose tolerance (Kamath, 2008).

3. **Polyphenols of cashew kernel testa:** The chemical nature of the polyphenols of cashew kernel testa has been determined by means of 2-dimensional paper chromatography. Presence of (+) catechin and (-) epicatechin as the major polyphenols has been confirmed by co-chromatography with authentic samples. Proanthocyanidins have been studied by treatment with hot acid and identification of the resultant anthocyanidins. Leucocyanidins and leucopelargonidins have been noticed as monomeric components, whereas polymeric proanthocyanidins contain in addition small quantities of leucodelphinidin. Individual components have been quantitatively estimated colorimetrically with Folin-Denis reagent, after separation by fractional extraction using solvents of increasing polarity and paper chromatography. The characteristic bluish-black discoloration noticed in cashew-nuts has been identified as an iron-polyphenol complex formed during processing. The polyphenols were found to be derived from the testa (Mathew, 1970).
4. **Studies on oleoresinous varnishes and their natural precursors:** Condensed tannins extracted from the seed testa of *Anacardium occidentale* is subjected to phytochemical and spectral studies such as UV and 13C NMR. Shell of *Cocus nucifera* on treatment with acid yields acid hydroxylates containing furfural which when condensed with tannins of *A. occidentale* form phenol–formaldehyde type resins. The spectral and physico-chemical properties of the resins are studied. Varnishes are prepared from these resins using linseed oil/linseed oil–tung oil. The service performances of the varnishes including their impedance spectra were evaluated. The results show that varnishes with good gloss and chemical resistivity can be prepared from these waste materials (Kumar, 2004).

5. **Plant regeneration through direct somatic embryogenesis:** A protocol of plant regeneration through direct somatic embryogenesis was established for the first time on cashew using seed coat explants. Embryos exhibited all stages of development, i.e. from globular to cotyledonary. Fifty percent of the embryos underwent conversion upon transfer to MS medium containing 4.65 mM kinetin and plantlets were successfully transferred to field conditions. Ninety percent survived in field conditions (Martin, 2003).
4.3 SCIENTIFIC REPORTS PUBLISHED FOR STEM BARK OF CASHEW

1. Genotoxicity and antigenotoxicity activity: The genotoxic and protective activities of cashew stem bark methanolic extract, in vitro was studied. Methyl methanesulfonate (MMS) was used as a positive control, to compare possible mechanisms of DNA damage induction in the Comet assay (Barcelos, 2007).

2. Gum exudates of cashew tree: Gum exudates from the Brazilian cashew-nut tree (*Anacardium occidentale* L.) contained traces of the reducing sugars, rhamnose (0.005%), arabinose (0.03%), mannose (0.007%), galactose (0.03%), glucose (0.02%), (0.05%), (0.008%) and (0.008%). The structure of this polysaccharide was determined and found to differ from the reports previously published for the gum of a tree growing in India, lacking units of 4-O-methylglucuronic acid (Menestrina, 1998).

3. Study on properties of Gum: The composition and solution properties of Indian and Papuan specimens of the gum from *Anacardium occidentale* have been studied and found to be closely similar. Contrary to earlier reports by Indian workers, this gum does not contain galacturonic acid. It does, however, contain glucose; this appears to be the first report of the presence of this sugar in a plant gum exudates (Douglas, 1974).

4. Mutagenicity and antimutagenicity of cashew stem bark: The mutagenicity and antimutagenicity of cashew stem bark methanolic extract (CSBME) on cell cultures of Chinese hamster lung fibroblasts (V79) was assessed. The data obtained in the chromosome aberrations (CA) test showed a significant reduction in CA frequency in the cultures treated with DXR and extract in comparison with those that received only DXR during the cell cycle phases G1 and S and throughout the entire cycle, as well as the absence of mutagenicity in all the treatments realized (Gustavo, 2007).

5. Enzymatic and inhibitory activities of cashew tree gum exudates: The gum exudate from the *Anacardium occidentale* tree has been analysed for carbohydrate, Kjeldahl nitrogen, protein and phenols, and for the activities of

6. **Structural analysis of the gum polysaccharide from *Anacardium occidentale***:
The gum exudate from *Anacardium occidentale* contains galactose (61%), arabinose (14%), rhamnose (7%), glucose (8%) and glucuronic acid (5%) in addition to small amounts (<2%) of each of mannose, xylose and 4-O methylglucuronic acid. Sequential Smith-degradations of *Anacardium occidentale* gum, and methylation analyses of the gum and of its degradation products indicated a highly-branched galactan framework consisting of chains of [beta]-(1-3)-linked D-galactose residues branched and interspersed with [beta]-(1-6) linkages (Anderson, 1975).

7. **Anti-inflammatory actions of tannins isolated from the bark of *Anacardium occidentale*** L.: A mixture of tannins (hydrolysable and non-hydrolysable) obtained from the bark of *Anacardium occidentale* L., on i.p. injection, demonstrated apparent anti-inflammatory activity in carrageenan- and dextran-induced rat paw oedemas, cotton pellet granuloma test and adjuvant-induced polyarthritis in rats. The tannins i.p. also inhibited acetic acid-induced 'writhing responses' in mice and were found to antagonise the permeability-increasing effects in rats of certain mediators of inflammation and to inhibit the migration of leucocytes to an inflammatory site (Mota, 1985).

8. **Sub-chronic Hepatotoxicity**: The phytochemical compositions and acute toxicity of the extract were determined. Toxicity profiles of the extract on some liver function parameters were evaluated following a sub-chronic oral administration at doses of 1.44 and 2.87 g/kg. The sub-chronic administrations of *Anacardium occidentale* inner stem bark extract did not significantly (p< 0.05) depress the function of hepatocytes in Wistar rats.

The (+)-cyanidanol-3 (made as CATERGEN, supplied by Zyma-Biogal Pharmaceutical Works, Debrecen, Hungary,) was is used as an antihepatotoxic and hepatoprotective drug in both men and animals against alcoholic and experimental liver injury. Ethanol was administered ad lib to CFY rats to cause mild alcoholic liver damage together with 200 mg/kg/day (+)-cyanidanol-3 to
CHAPTER 4  REVIEW OF LITERATURE

prevent the tissue. The (+)-cyanidanol-3 prevents changes and the morphometric parameters in the treated group were almost the same as in the controls. The treatment with (+)-cyanidanol-3 alone does not affect the hepatic tissue parameters. The results show the hepatoprotective effect of (+)-cyanidanol-3 and the suitability of the morphometric method for quantitative comparison of normal and experimentally-altered liver cells. (Varga, 1989; Ryle 1981; and Ryle 1983).

9. **Stimulation of glucose uptake in C2C12 muscle cells by cashew extracts:** The anti-diabetic properties of cashew plant parts were studied using differentiated C2C12 myoblasts (myotubes) and rat liver mitochondria. Hydroethanolic extract of cashew seed (CSE) and its active component, anacardic acid (AA), stimulated glucose transport into C2C12 myotubes in a concentration-dependent manner. Extracts of other parts (leaves, bark and apple) of cashew plant were inactive (Tedong, 2010).

10. **Effects on in vivo inflammatory models:** The methanol extract of *Anacardium occidentale* stem bark was evaluated for activities against the lipopolysaccharide (LPS)-induced septic shock, as well as LPS-induced microvascular permeability in mice. Pre-treatment with *Anacardium occidentale* extract (25-200 mg/kg) caused a dose-dependent and significant (p <0.05) reduction in the elevated levels of alanine and aspartate aminotransferases in the sera of D-galactosamine-primed mice injected with LPS. A dose-related inhibition of LPS-induced microvascular permeability in mice was also produced by pentoxifylline, and the extract (Olajide, 2004).

11. **Hypoglycaemic effect of stigmast-4-en-3-one and its corresponding alcohol:** Intravenous administration of the hexane extract of the bark of *Anacardium occidentale* (cashew) in normal, healthy dogs produced a significant lowering of the blood glucose levels. Pursuit of the hypoglycaemic principle(s) in the hexane extract resulted in the isolation and characterization of two compounds, stigmast-4-en-3-ol and stigmast-4-en-3-one (Alexander, 2004).
4.4 SCIENTIFIC REPORTS PUBLISHED FOR ROOTS OF CASHEW

1. Hypoglycemic potencies of crude ethanolic extracts of cashew roots: The crude ethanolic extract of cashew root and pawpaw fruits showed hypoglycemic potencies, however, the crude ethanolic extract of cashew roots showed more hypoglycemic potency than the crude extract of pawpaw fruits in both guinea pigs and rats. The work concludes that ethanolic extract of cashew root and pawpaw fruit contains natural substances that can be harnessed for the treatment and management of diabetes mellitus (Egwim, 2005).

4.5 SCIENTIFIC REPORTS PUBLISHED FOR CASHEW NUT SHELL OIL

1. Gastroprotection activity: The gastroprotection effect of anacardic acids against the ethanol-induced gastric damage was studied to examine the underlying mechanism(s). Gastroprotection was assessed in relation to inhibition of gastric lesion area. These results suggest that anacardic acids afford gastroprotection principally through an antioxidant mechanism, activation of capsaicin-sensitive gastric afferents, stimulation of endogenous prostaglandins and nitric oxide, and opening of K+ATP channels (Talita, 2010).

2. Supercritical fluid extraction of cashew nut shell liquid: Nut shell liquid can be separated from fragmented honeycombed cashew shell material without employing thermal techniques with a pressure profile method that uses supercritical carbon dioxide as solvent. Using the method, extraction yields of cashew nut shell liquid (CNSL) of up to 10 times than those obtained by usual supercritical fluid extraction were achieved. Analysis with liquid chromatography of the extracts contained approximately 50 mol% anacardic acids, 29 mol% cardols, and 21 mol% cardanols including mono-, di-, and tri-ene constituents (Setianto, 2009).

3. Phenolic constituents of natural cashew nut-shell liquid: The phenolic constituents of natural cashew nut-shell liquid (CNSL) from Anacardium occidentale have been separated by high-performance liquid chromatography by the reversed-phase method. The relative molar response values for the saturated
component phenols have been determined and the use of an internal standard has led to a quantitative procedure (Tyman, 1984).

4. **Cashew nut allergy**: It is the second most commonly reported tree nut allergy in the United States. The cloned allergen, designated Ana o 3, was identified as 2S albumin. MALDI-TOF mass spectroscopy of native Ana o 3 yielded a molecular mass of 12,598 d. This 2S albumin protein is a major allergen in cashew nut and demonstrates a possible basis for cross-reactivity with walnut 2S albumin (Jason, 2005).

5. **Compositional studies on nut shell oil**: An extensive gas chromatographic investigation of alternative stationary phases to polyethyleneglycol adipate which are suitable for the quantitative analysis of hydrogenated and methylated natural and technical cashew nut-shell liquid. A comparison has been drawn between the ionisation processes in the flame ionisation detector and in mass spectrometry (Tyman, 1977).

6. **Spectroscopic and chromatographic analysis**: Natural cashew nut-shell liquid has been analysed by thin-layer chromatography (TLC) combined with spectrophotometry. In a direct method the bands were examined in situ by an adsorbance method involving a 'flying spot' scanning procedure and densitometry (Tyman, 1978).

7. **Gas–liquid chromatography analysis of nut shell oil**: Cashew nut-shell liquid (CNSL) of natural origin or as the technical product obtained by industrial decarboxylation, has been analysed by gas–liquid chromatography (Tyman, 1976).

8. **Supercritical extraction of nut shell oil**: The separation of CNSL from the pericarp of the cashew nut with supercritical carbon dioxide was carried out. The pressure profile extraction method proposed in this work increases the possible CNSL extraction yields and greatly reduces the amount of CO2 required for CNSL separation (Smith, 2003).
9. Crosslinked materials from cashew gum: Cashew gum (CG) and carboxymethylated CG (CMCG) were synthesized using epichlorohydrin (E) as the crosslinking agent. The products were characterized by 13C nuclear magnetic resonance, IR spectroscopy, swelling degree and thermal analysis (Durcilene, 2006).

10. Degradation products of carotenoid degradation: The influence of organic acid and heating treatments on carotenoid degradation on a simulated cashew apple juice was assessed by high performance liquid chromatography coupled with a photodiode array and mass spectrometry detectors. The facts indicated that isomerisation and oxidation to both coloured and non-coloured compounds were the main reactions occurring during heating of carotenoids in aqueous-based and juice systems (Leila, 2009).

11. Phenolic lipid composition during development of cashew: Quantitative composition of the major phenolic lipids (anacardic acids, cardols and cardanols) of the apple, kernel and shell of the cashew plant have been determined at various stages of development by high-performance liquid chromatography (Shobha, 1992).

12. Quantitative analysis of the phenolic lipids: The novel separation of the constituent phenols in technical cashew nut-shell liquid from the industrial processing of *Anacardium occidentale* has been effected by high-performance liquid chromatography. Gradient elution with tetrahydrofuran and acetonitrile has also enabled the polymeric material to be estimated in the various types of technical cashew nut-shell liquid examined (Tyman, 1981).

13. Promoting action of cashew nut shell oil mouse skin tumour model: The commercially available oil derived from the shell of cashew nut (*Anacardium occidentale*) was tested for its potency in promoting the DMBA-initiated cells into papillomas in a murine two-stage skin tumorigenesis model system. Few speculative mechanisms for the observed effect of cashew nut shell oil on initiated skin are discussed (Banerjee, 1992).
14. Antioxidant properties and chemical composition of technical cashew nut shell liquid (tCNSL): The antioxidant activity of the technical cashew nut shell Liquid (tCNSL) using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging assay and the xanthine oxidase assay, as well as in vivo evaluation by Saccharomyces cerevisiae assay. Also, the chemical composition of tCNSL was determined by gas chromatography-mass spectrometry (GC-MS) (Teresinha, 2011).
4.6 SCIENTIFIC REPORTS PUBLISHED FOR CASHEW SHOOTS

1. **Free Radical scavenging activity of cashew shoots:** The total phenolic content and antioxidant activities of methanol, hexane and ethyl acetate extracts of the shoots of *Anacardium occidentale* were measured. Total phenolic content was assessed by the Folin-Ciocalteau assay whereas antioxidant activities were assessed by measuring the ability of the extracts to scavenge the ABTS<sup>+</sup> and DPPH<sup>•</sup> radicals, superoxide anion radicals and nitric oxide radicals as well as their ability to reduce ferric ions. The order of the antioxidant potency of the plant extract is methanol > ethyl acetate > hexane. The methanol extract contained more than 7 fold of total phenolic content compared to the hexane and ethyl acetate extracts indicating the likely possibility that the observed antioxidant activities were partly contributed by the phenolics (Nurhanani, 2008).

2. **In vitro adventitious shoot formation from cotyledon explants of cashew:** Excised cotyledons from mature embryos of cashew (*Anacardium occidentale* L.) developed adventitious shoots from the proximal end when cultured on Murashige and Skoog's (MS) medium. About 55% of in vitro raised shoots developed roots. This procedure was first applicable to the three commercial high-yielding cultivars of cashew (Ananthakrishnan, 2002).
4.7 SCIENTIFIC REPORTS PUBLISHED FOR CASHEW APPLE

1. **Determination of Flavonoids**: Liquid chromatography, with diode array detection and electrospray ionization mass spectrometry (LC-DAD-ESI/MS), was used to identify and quantify flavonoids in cashew apple. One anthocyanin and thirteen glycosylated flavonols were detected in a methanol-water extract. (Sousa, 2007).

2. **Characterisation of residues in peduncle bagasse**: The characterization of the incineration ashes of the primary residue derived from the cashew's juice extraction, the peduncle bagasse. Measurements showed that these ashes represent only 3% of the incinerated material. EDX analysis indicated the presence of the following elements: C, O, P, K, Mg, S, Na, Al and Si. X-ray diffraction and thermal analyses pointed $\text{KHCO}_3$ (54.17%), $\text{K}_2\text{SO}_4$ (34.08%) and $\text{MgKPO}_4 \cdot 6\text{H}_2\text{O}$ (10.06%) as the most significant crystalline phases (Ricardo, 2007).

3. **Determination of constituents of skin and flesh of cashew apple**: Monomeric phenols were extracted by acetone/water (60:40) from the skin and flesh of four cashew apple genotypes from Brazil and Benin (West Africa), purified by absorption chromatography and subjected to HPLC-DAD/ESI-MS analysis. Skins were found much richer than fleshes in simple phenolics (Laetitia, 2009).

4. **Determination of volatile components in cashew apple**: An essence of fresh cashew ‘apple,’ was analysed by GC and by GC/MS using both EI and CI techniques. The fruit produced a very small quantity of aroma volatiles (ca 3.6 [µ]/kg fresh fruit), much less than that obtained from most similar tropical fruits. Five aldehydes comprised ca 26% of the sample, but terpene hydrocarbons (38%) provided the major group of compounds (Alexander, 1982).

5. **Carotenoids and ascorbic acid from cashew apple**: The levels of carotenoids were analysed in red and yellow cashews from the Southeast and Northeast, respectively. The total carotenoid levels of the rounded red fruits were 1.5 and 1.7 times lower than those found in the yellow and red varieties, respectively, all being from the Northeast region. Yellow fruits from the Northeast presented 1.7
times higher provitamin A levels than those from the Southeast whereas, for the red variety, the values were similar (Raquel, 2003).

6. Essential oils of the leaves, fruits, and flowers cashew: Essential oils of various parts of yellow and red variety of (*Anacardium occidentale* L.) were obtained by hydrodistillation and analysed by GC/MS. The oil of the leaves from red cashew was dominated by (E)-[beta]-ocimene (28.8%), [alpha]-copaene (13.6%), and[delta]-cadinene (9.1%). The major constituents of the oil from fruits of the red variety were palmitic (19.6%) and oleic (19.6%) acids, while palmitic acid (11.4%), furfural (10.0%), 4-hydroxydodecanoic acid lactone (8.2%), (E)-hex-2-enal (7.2%), (Z)-hex-3-enol (6.2%), and hexadecanol (6.2%) were the principal components identified in the oil of yellow cashew. The main constituents found in the oil of the flowers of red cashew were [beta] -caryophyllene (26.0%), methyl salicylate (12.8%), and benzyl tiglate (11.3%) (Jose, 2000).

7. Antioxidant capacity of cashew apple: The content of anacardic acids, cardanolS and cardols in cashew apple, nut (raw and roasted) and cashew nut shell liquid (CNSL) were analysed. A mixture of anacardic acids (10.0 mg/ml) showed the higher antioxidant capacity (IC$_{50}$ = 0.60 mM) compared to cardols and cardanols (IC$_{50}$ > 4.0 mM). The antioxidant capacity of anacardic acid-1 is more related to inhibition of superoxide generation (IC$_{50}$ = 0.04 mM) and xanthine oxidase (IC$_{50}$ = 0.30 mM) than to scavenging of hydroxyl radicals (Trevisan, 2006).

8. Antioxidant activity of anacardic acids: Anacardic acids, 6-pentadec(en)ylsalicylic acids isolated from the cashew *Anacardium occidentale* L. (Anacardiaceae) nut and apple, were found to possess preventive antioxidant activity while salicylic acid did not show this activity. Anacardic acids act as antioxidants in a variety ways, including inhibition of various prooxidant enzymes involved in the production of the reactive oxygen species and chelate divalent metal ions such as Fe2+ or Cu2+, but do not quench reactive oxygen species. The C15-alkenyl side chain is largely associated with the activity (Kubo, 2006).

9. Design and evaluation of anacardic acid derivatives as anticavity agents: On the basis of antibacterial effect of anacardic acids, 6-pentadecenylsalicylic acids,
isolated from the cashew apple, *Anacardium occidentale* L. (Anacardiaceae), a series of 6-alk(en)ylsalicylic acids were synthesized and tested for their antibacterial activity against *Streptococcus mutans* ATCC 25175. Among them, 6-(4',8'-dimethylnonyl)salicylic acid was found to exhibit the most potent antibacterial activity against this cariogenic bacterium with the minimum inhibition concentration (MIC) of 0.78 µg/ml (Green, 2008).

10. **Cell proliferation inhibitory and apoptosis-inducing properties of anacardic acid in human breast cancer MDA-MB-231 cells:** Anacardic acid and lunasin are two plant-derived compounds that show inhibitory effects on cell proliferation and inducing properties of apoptosis in human breast cancer MDA-MB-231 cell line. Both lunasin and anacardic acid exert their effects through the modulation of expression of several genes involved in cell cycle, apoptosis and signal transduction. The results introduce these two compounds as a promising strategy to prevent/treat breast cancer (Hsieh, 2011).

11. **Characterization of anacardic acids by micellar electrokinetic chromatography and mass spectrometry:** Capillary electrophoresis for separation of anacardic acids (6-alkylsalicylic acids) has been studied. Separation of anacardic acids were achieved in the polydimethylacrylamide-coated capillary using 10 mM phosphate background electrolyte pH 6.5 with addition of 1 M urea, 20% acetonitrile, 10 mM of [beta]-cyclodextrin and 1 mM of heptakis-6-sulfo-[beta]-cyclodextrin. Mass spectrometry was used for the identification of anacardic acids in the extract from cashew nuts in single and tandem mode using Q-TOF instrument (Cesla, 2006).

12. **Flavonols in fresh and processed fruits:** Flavonols (myricetin, quercetin and kaempferol) and flavones (luteolin and apigenin) were determined in Brazilian fruits, using a previously optimized and validated HPLC method. The best sources of flavonols among the fruits investigated were pitanga, cashew-apple, acerola and apple, the first three being analyzed for the first time (Ribani, 2009).

13. **Study on antioxidant activity of dry fruits:** The antioxidant activity of cashew nut through several chemical and biochemical assays: reducing power, lipid
peroxidation damage in biomembranes, determination of antioxidant enzymes activity (SOD and CAT) was carried out. The higher phenolic content was found in walnuts followed by almonds cashew nut, chironji and least phenolic content was found in raisins (Mishra, 2010).

14. **Glycaemic effects in normal and streptozotocin diabetic mice**: The traditional treatment of diabetes mellitus in northern Europe was studied using normal and streptozotocin diabetic mice to evaluate effects on glucose homeostasis. Cashew leaves were administered in the diet (6.25% by weight) and/or as decoctions or infusions in place of drinking water, to coincide with the traditional method of preparation. Treatment was given for 28 days. After administration of streptozotocin (200 mg/kg) cashew, did not significantly affect the parameters of glucose homeostasis studied (basal glucose and insulin, insulin-induced hypoglycaemia, glycated haemoglobin and pancreatic insulin concentration). (Swanston, 1989).
4.8 SCIENTIFIC REPORTS PUBLISHED FOR FLOWERS OF CASHEW

**Pollen allergy in patients with asthma:** Upon exposure to cashew pollen the patients in study, (40%) had positive skin test reactions in various grades. About 90.9% patients had a positive bronchial provocation tests (BPT) result, and the majority of patients had grade III and grade IV reactions. This study provided us with knowledge of an additional pollen, *Anacardium occidentale*, which could trigger an asthmatic response in allergic individuals (Fernandes, 1995).

4.9 PATENTS PUBLISHED FOR CASHEW, CATECHIN, AND CYANIDANOL

- A United States patent is also published regarding the process of coating cashew nut with intact testa in order to make it edible. As a part of the processing of cashew nuts a process was designed to coat the cashews (with testa) with flavours, spices, honey and sugar infusions (Harikrishnan, 2005).

- A patent to control the isomerisation of (-)-epicatechin and (+) – catechin and their altered monomers in edible products was published. The process involves use of open food processor under reduced oxygen pressure or a closed vessel (Hammerstone, 2007, 2010).

- A United States patent related to pharmaceutical preparations containing (+)-cyanidanol-3-ol derivates, particularly suitable for treating liver and venous diseases at the dose range between 10-500 mg/kg in rats is reported (Ballenegger, 1987).