Kawas et al. 1997). A cholinesterase inhibitor tacrine combined with estrogen may have a greater therapeutic effect (Schneider 1995).

Abnormal phosphorylated fibrillary proteins, which aggregate in the neuronal cytoplasm, are called neurofibrillary tangles. Neurons, which are very complex with their branching structures, have to maintain a healthy cytoskeleton system, but the failure of this causes the tangle formation (Munoz and Feldman 2000). Neurofibrillary tangles are highly accumulated in the hippocampus, which is primarily involved in the storage of permanent memories. The basal forebrain that provides the cholinergic innervations to the cortex is also equally affected, resulting in severe neurodegeneration (Munoz and Feldman 2000).

Senile plaques are complex and made up of a sugar polymer component called glycosaminoglycans, which aids in the assembly of the beta-amyloid (Aβ) of the transmembrane protein. Senile plaque deposition will start slow, but it eventually builds up through an orderly, sequential manner which finally develops into AD (Mackenzie 1994). The amount of senile plaque will increase with age. Butyrylcholinesterase may also play an essential role in the maturation process of the plaques (Guillozet et al. 1997).

Familial AD, which is a kind of autosomal dominant disease caused by point mutation of the gene coding for Aβ precursor protein, is located on chromosome 21. The mutation causes varied effects on the formation of the protein Aβ, sometimes as a long amino acid chain or vice-versa. Other genes include the genes which code for presenilin 1 and presenilin 2 proteins, which also accounts for familial AD (Gomez-Isla et al. 1997). Both Aβ precursor proteins and presenilin 1 and 2 proteins are helpful in organising vesicular trafficking (Beyreuther and Master 1997). Other major causative factors for AD includes accidents and severe head trauma (Schofield et al. 1997). Patients who suffer from severe epilepsy have a very high risk of developing senile plaques at a younger age than the normal population (Mackenzie and Miller 1994).

9.2 THERAPEUTIC STRATEGIES FOR AD

AD pathology displays multifactorial and complex pathways (Small and Mayeux 2005). Pharmacological interventions on all these factors and pathways were investigated, and more are being discovered as the years unfold. These possible mechanisms could be intervened with plants and their derivatives to prevent and treat AD.

9.2.1 Aβ and Senile Plaque

Secretases play an important role in the formation of senile plaques as a result of proteolytic cleavage of the amyloid precursor protein (APP) into Aβ – a primary component of senile plaques. Aβ aggregation and deposition leads to neurodegeneration (Castro et al. 2002). Plant derivatives are capable of intervening in the formation and deposition of Aβ fibrils, and the clearance of senile plaques are possible therapeutic approaches in AD.

9.2.2 Secretases

APP processing involves two pathways – amyloidogenic and non-amyloidogenic. β-secretase and γ-secretase of the amyloidogenic pathway cleave the extracellular