ABSTRACT

Natural products either obtained from plants or other biological sources are expected to give better and promising anticancer agents. A lot of researches have indicated that curcumin can treat cancer. Curcumin is a polyphenol compound derived from the plant of *Curcuma longa*, called as turmeric. It is known that curcumin induces many signal transduction pathways in cancer, including the apoptotic pathway. But the weaknesses of curcumin—low bioavailability and rapid clearance—hinder its potency. A lot of synthetic analogues of curcumin have been developed to tackle these problems. This study aims to explain the synthetic procedure of curcumin analogues which induces apoptosis and evaluates the apoptotic mechanism.

This narrative review was conducted by finding research articles in electronic journal databases. It was done by inserting various keywords such as "synthetic curcumin analogues", "synthesis of curcumin analogues", "apoptotic pathways", "apoptosis", "death ligand", and "death receptors". A number of articles that fulfill the inclusion criteria were selected. Selected articles were then analyzed and made into a narrative review.

The result shows that modifications of 30 synthetic curcumin analogues that have been reviewed vary: aromatic side chain with 1 analogue, carbon linker chain with 2 analogues, diketo functionality with 4 analogues, monocarbonyl with 20 analogues, and active methylene group with 3 analogues. The synthesis procedure of the analogues was mostly done using aldol condensation method, while the most used starting material was the combination of substituted benzaldehydes and ketones. It was found that all synthetic curcumin analogues possess more stable compounds and demonstrate better bioavailability than curcumin. The apoptotic mechanisms present in the analogues were ROS generation and ER-stress induced apoptosis with 14 analogues, mitochondrial dysfunction with 9 analogues, cell cycle arrest with 8 analogues, Akt/mTOR pathway inhibitor with 3 analogues, apoptotic proteins regulation with 10 analogues and caspases activation with 18 analogues.

Keywords: Curcumin analogues, Synthetic, Synthesis Process, Anticancer, Apoptosis