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Pinoradiol®, the plant derived polyphenolics targets growth inhibition of human breast cancer cells through induction of oxidative stress mediated lysosomal membrane permeabilization (LMP)

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Polyphenols are abundant non-nutrients in our diet as they are present in the fruits, vegetables, cereals, beverages and tea. Several epidemiological studies have repeatedly shown an inverse relationship between the risk of cancer development and the consumption of polyphenols rich diet. Polyphenols targets cancer cells by various mechanisms such as estrogenic or antiestrogenic activity, antiproliferation, induction of cell cycle arrest or apoptosis, suppression angiogenesis, regulation of the host immune system and cellular signalling pathways. In the present study, we report a novel mechanism of action of the polyphenolic mixtures,Pinoradiol® studied against breast cancer which is one of the most prevalent cancer types among women worldwide at present, using human cancer cell lines. First, we observed that Pinoradiol® induced an extensive cytoplasmic vacuolation in breast cancer cells, MCF-7. Those vacuoles were mostly caused by lysosomal dilation evidenced by reduced acridine orange red and lysotracker green fluorescence intensity, and cytosolic distribution of lysosomal aspartyl protease, cathepsin-D. Mechanistic investigations revealed that Pinoradiol® induced increased production of ROS was responsible for the loss of lysosomal membrane integrity evidenced from improved lysosomal function in the presence of an antioxidant, n-acetylcysteine. Next we found that Pinoradiol® induced breast cancer cell death was independent of caspases. Moreover, Pinoradiol® caused an accumulation of LC-3 and its associated protein, p62, confirming the blockade of autophagic flux at the maturation stage, which might be the loss of lysosomal function. Collectively, our study reveal a novel mechanism underlying Pinoradiol® induced breast cancer cell death involving ROS mediated lysosomal membrane permeabilization.

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Biography:

Dr. Young-Kyoon Kim is from the Department of Forest Products and Biotechnology and he is the Dean of College of forest Science. He has served as a professor in Kookmin University since 1994. He is also the Principal Investigator of Forest material Bioindustrialization Research Center, Forest Science & Technology, Korea. He worked as a Research Scientist in the US Department of Agriculture, Agricultural Research Service (USDA-ARS),Western Regional Research Center (WRRC), Albany, California (2011-2012). He also worked in Scripps Institution of Oceanography, University of California, San Diego, La Jolla (1992-1994). He received a B.A. from the Kangweon National University in 1985, and M.A. from Seoul National University in 1987, and a Ph.D. in Natural Products from University of California at Berkeley in 1992.