SCAPE OF THE STUDY
Hepatocellular carcinoma (HCC) is the fifth most common form of cancer occurring worldwide and is the third most common cause of cancer-related deaths. The development of HCC is a multistep carcinogenesis process, commonly associated with the deregulation of cell signaling such as Hippo signaling. Thus, targeted therapy can decelerate HCC progression by specific inhibition of alternated signaling cascades. In recent years, the influence of Hippo signaling in the pathogenesis of liver diseases has sparked great interest in developing potential therapeutics that could target key effectors of this signaling cascade. In HCC, liver cancer cells frequently exhibit hyperactive Yap expression due to inactivation of Hippo signaling, suggesting that Yap is a central contributor to tumourigenesis (Zhao et al., 2007). Hence, an approach for the activation of Hippo signaling by increasing the activities of Mst1/2 and/or Lats1/2 kinases functioning upstream of Yap/TAZ could provide valuable evidence for the development of novel drugs. Earlier studies in this laboratory have revealed the hepatoprotective effects of morin, a dietary flavonoid with a broad spectrum of biological activities, including inhibition of cell proliferation, induction of apoptosis, alteration of the activity of certain intracellular enzymes and antioxidant properties, favoring anticancer properties through multifactorial pathways. Therefore, in this study, it is proposed that morin may mediate its regulatory role through activation of Hippo pathway in progression of HCC.

Study Objectives

Objective 1: To elucidate the anti-proliferative and pro-apoptotic effects of morin in HepG2 cells.

Objective 2: To understand the molecular regulatory mechanism of morin behind the activation/inhibition of key molecular pathways in the progressive stages of experimental liver cancer.

Objective 3: To elucidate the molecular mechanisms behind the activation of Hippo pathway by morin in Mst1 transfected HepG2 cells.