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Abstract - Master Thesis Project, the Pharmacy Programme

Caffeine and analogues as potential drugs for Hepatocellular carcinoma

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Hepatocellular carcinoma (HCC) is a primary liver cancer and the third most common cause of cancer mortality worldwide. Surgery is the most effective treatment for HCC, either hepatic resection or liver transplantation. Nevertheless, only a small number of HCC patients qualify for surgery or transplantation. At present, there is no proven effective systemic chemotherapy for HCC. Therefore there is a specific need to develop novel and more efficient drugs. To achieve this it is important to understand the mechanisms of HCC development and progression and identify key molecules involved in this process. Several signalling pathways are deregulated in HCC including the pathway activated by the lipid kinase phosphoinositide 3-kinase (PI3K) and the serine/threonine kinase, protein kinase B (PKB, a.k.a. Akt). Data accumulated in the last decade have established that this pathway plays a key role in cancer development and progression. Interestingly, several recent studies have identified an association between coffee/caffeine intake and reduced risk of HCC. In the present study we have investigated whether caffeine and its analogue CGS 15943 have an anti-carcinogenic effect on HCC and if they exert their anti-carcinogenic effect via blocking the PI3K/Akt pathway *in vitro*. Our data showed that caffeine and CGS 15943 had an anti-carcinogenic effect on HCC and this effect was shown to be interfering with PI3K/Akt pathway. Our data reveal that caffeine and other analogues may be promising agents for the chemoprevention and treatment of HCC.