Histopathological evaluation revealed that one of the patients had a non-germ cell tumor, a Sertoli cell tumor, while others had mixed germ cell tumors. Half of them had only a single right frontoparietal lesion (21 mm) or right occipital (42 mm), both were heterogeneous in T1WI and T2WI, and with intense and heterogeneous enhancement with gadolinium. The other two patients had multiple lesions. One of them had left frontoparietal (2.2 mm, hyperintense in T1) and right occipital (1.8 mm, hypointense in T1) lesions, both heterogeneous and predominantly hypointense in T2 and T1WI with no enhancement. The other had right temporal (5 mm) and left occipital (11 mm) lesions, both isointense in T1WI and T2WI with intense and homogeneous enhancement. There was no diffusion restriction in all three cases and all four cases were hypointense in T2*. 

Conclusion: Although the imaging features of brain metastases differ in some aspects, they all have a hemorrhagic component and a very low survival rate after diagnosis.

References

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Synthesis and tumor cell growth inhibitory effects of the marine product analogues of fiscalin B

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Aim: The aim of this work was to synthesize fiscalin B, to pursue the development of a library of derivatives and to investigate the derivatives for their potential antitumor activity.

Introduction: Marine organisms provided numerous novel compounds with sensational multiple pharmacological properties. The necessity of novel therapeutics has gain more importance especially because of the resistance associated to the current therapeutics and the inexistent treatments for incurable diseases. Fiscalin B is a fungal metabolite with a pyrazino[2,1-b]quinazoline-3,6-dione system reported to have significant biological activities.

Methods: Two methods were studied for synthesis — double cyclization and microwave assisted procedures. First method started with coupling reactions to form tripeptide of tryptophan methyl ester linked to N-Fmoc-valine via anthranilic acid. Then, the dehydrative cyclization was performed using formamide to form the intermediate oxazine. The coupling reaction to form the fiscalin B were achieved after deprotection. The second method is the coupling of anthranilic acid with N-Boc-valine to form Boc-protected benzoazin-4-one by thermal heating conditions. Then, the addition of tryptophan methyl ester hydrochloride led to 4-quinazoline-3,6-dione scaffold by microwave irradiation. The cell growth inhibitory effect was investigated by the SulforhodamineB assay.

Results: The use of amino acids with different configurations and different side chains or even the derivatization of the existing functional groups were enable the application of this synthetic methodology for a library of fiscalin B analogues. The formation yields of fiscalin B analogues were low, ranging from 3 to 16%. Eight derivatives were tested on non-small cell lung cancer (H460), colon adenocarcinoma (HCT15) and breast cancer (MCF7) human cell lines and showed moderate cytotoxic effects, with GI50 concentrations ranging from 30 to 80 µM.

Conclusion: Significant differences were obtained between enantiomeric pairs.

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References

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