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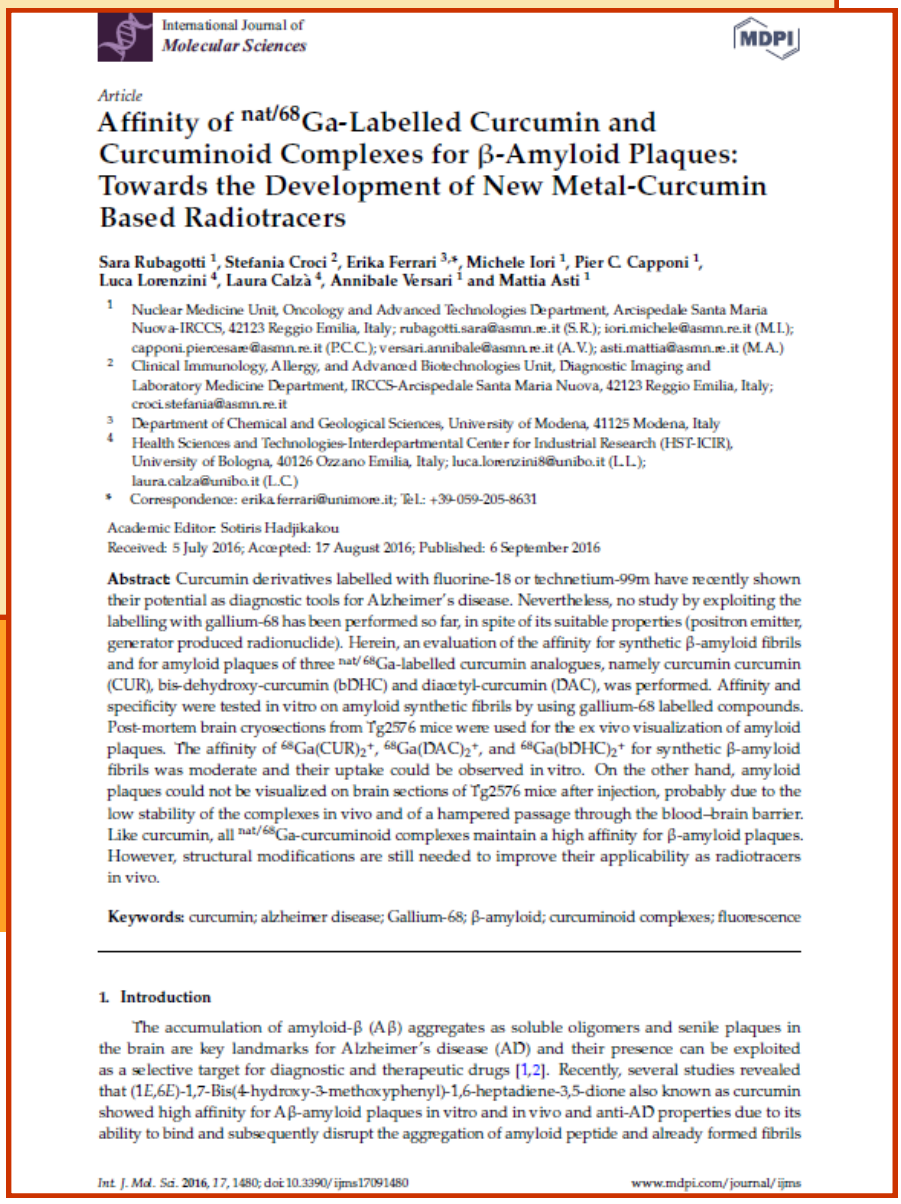

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Article

Affinity of $^{nat/68}$Ga-Labelled Curcumin and Curcuminoid Complexes for β-Amyloid Plaques: Towards the Development of New Metal-Curcumin Based Radiotracers

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Abstract: Curcumin derivatives labelled with fluorine-18 or technetium-99m have recently shown their potential as diagnostic tools for Alzheimer's disease. Nevertheless, no study by exploiting the labelling with gallium-68 has been performed so far, in spite of its suitable properties (positron emitter, generator produced radionuclide). Herein, an evaluation of the affinity for synthetic β-amyloid fibrils and for amyloid plaques of three $^{nat/68}$Ga-labelled curcumin analogues, namely curcumin curcumin (CUR), bis-dehydroxy-curcumin (bDHC) and diacetyl-curcumin (DAC), was performed. Affinity and specificity were tested in vitro on amyloid synthetic fibrils by using gallium-68 labelled compounds. Post-mortem brain cryosections from Tg2576 mice were used for the ex vivo visualization of amyloid plaques. The affinity of ^{68}Ga(CUR)$_2^+$, ^{68}Ga(DAC)$_2^+$, and ^{68}Ga(bDHC)$_2^+$ for synthetic β-amyloid fibrils was moderate and their uptake could be observed in vitro. On the other hand, amyloid plaques could not be visualized on brain sections of Tg2576 mice after injection, probably due to the low stability of the complexes in vivo and of a hampered passage through the blood–brain barrier. Like curcumin, all $^{nat/68}$Ga-curcuminoid complexes maintain a high affinity for β-amyloid plaques. However, structural modifications are still needed to improve their applicability as radiotracers in vivo.

Keywords: curcumin; alzheimer disease; Gallium-68; β-amyloid; curcuminoid complexes; fluorescence

1. Introduction

The accumulation of amyloid-β (Aβ) aggregates as soluble oligomers and senile plaques in the brain are key landmarks for Alzheimer's disease (AD) and their presence can be exploited as a selective target for diagnostic and therapeutic drugs [1,2]. Recently, several studies revealed that (1*E*,6*E*)-1,7-Bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione also known as curcumin showed high affinity for Aβ-amyloid plaques in vitro and in vivo and anti-AD properties due to its ability to bind and subsequently disrupt the aggregation of amyloid peptide and already formed fibrils