Mitsuji Yamashita et al., Der Pharmacia Sinica 2019, Volume:10
DOI: 10.21767/0976-8688-C1-001

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Euroscicon Conference on
Medicinal Chemistry and Biosimilars
March 25-26, 2019 | Budapest, Hungary

# PRECLINICAL RESEARCHES ON TUMOR ACCUMULATIVE NOVEL SUGAR DENDRITIC GD-DTPA COMPLEX MRI CONTRAST AGENTS AND IER5/CDC25B TAGETED NOVEL PHOSPHA SUGAR MOLECULAR TRGETED ANTITUMOR AGENTS TO INNOVATE IN CANCER THERAPY

Innovative and strategic materials against tumor to decrease sharply the number of people died by tumors are desired eagerly. To innovate in medical technologies of diagnosis and cure for various kinds of cancers by novel medicinal materials, i.e., sugar dendritic Gd-DTPA complex MRI contrast agent (DEN-OH) and IER5/Cdc25B targeted novel molecular targeted phospha sugar antitumor agents (e.g., TBMPP) were prepared and evaluated in vitro and in vivo methods, and then these novel medicinal materials were revealed preclinically to have excellent characters against tumor cells. Sugar dendritic Gd-DTPA complex (DEN-OH) was prepared by introduction of protected sugar dendritic parts to diethylenetriamine pentaacetic acid (DTPA) ligand followed by the successive complex formation with Gd (III) and hydrolysis. The prepared DEN-OH for MRI contrast agent (1/10 Gd concentration compared with Magnevist) showed quite clearer images of quite early stage of cancer (Figure 1). Phospha sugar derivatives, one of pseudosugar derivatives (Figure 2), were prepared via traditional or newly developed synthetic pathway to construct the compound library. Deoxybromophospha sugar derivatives (e.g., TBMPP) prepared from phospholenes were first found to exert quite effective and wide spectral antitumor activities by in vitro evaluation against various kinds of leukemia cells such as K562 and U937 cell lines as well as solid cancer cells (stomac, lung, and skin cancers), where normal cells were not suffered from any damages. Mechanistic studies of phospha sugar (TBMPP) on leukemia cells by Western blotting showed that the phospha sugar enhanced the expression of IER5, and then suppressed the expression of Cdc25B in the cell cycle of tumor cells. As the results, tumor cells might selectively and specifically might be induced apoptosis at the mitosis step of the tumor cell cycle. In vivo evaluation for TBMPP was successfully performed by using a nude mouse transplanted by K562 cells on the skin (Figure 3)

## Biography

Mitsuji Yamashita has completed his PhD from Nagoya University, Japan, and Postdoctoral studies from Toyota Science and Chemistry Research Center, Japan, and Iowa State University, USA, as well as a Visiting professor of University of Massachusetts, USA, and a Visiting researcher of Oxford University, UK. He was a Professor of Shizuoka University, Japan, and he was retired at his age of 65 years old followed by the university regulation. After the retirement, he was a Special Professor and Guest Professor of Shizuoka University. He is now a Professor Emeritus of Shizuoka University and a part time Lecturer of Shizuoka Science and Engineering University, Japan, and established a private research institute named "Research Institute for Innovative and Strategic Materials of Medicinal Technology against Tumors". He has published more than 180 papers in journals and patents (more than 80 open patents and 38 registered patents).

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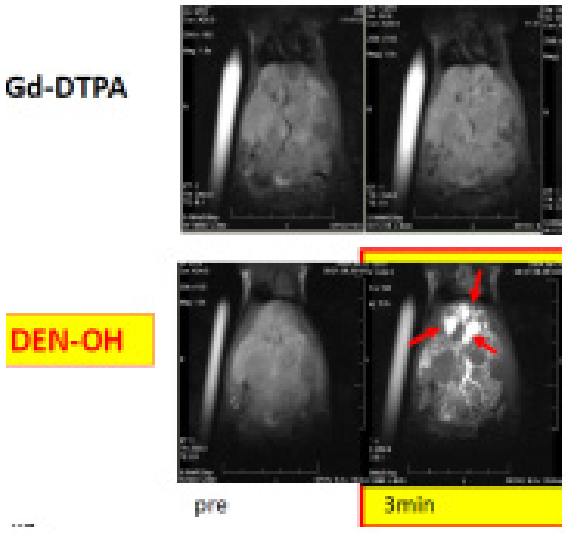


**Figure 1:** MRI of liver cancer of a Rat with Gd-DTPA (Magnevist) (Top) and DEN-OH (Bottom)

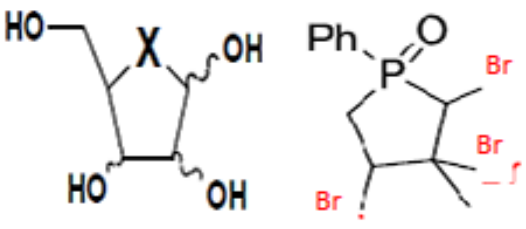


**Figure 2:** Pseudo sugars (X = NH, P (O) R, etc. (Left)); Branched deoxytribromo-phospha sugar TBMPP (Right).

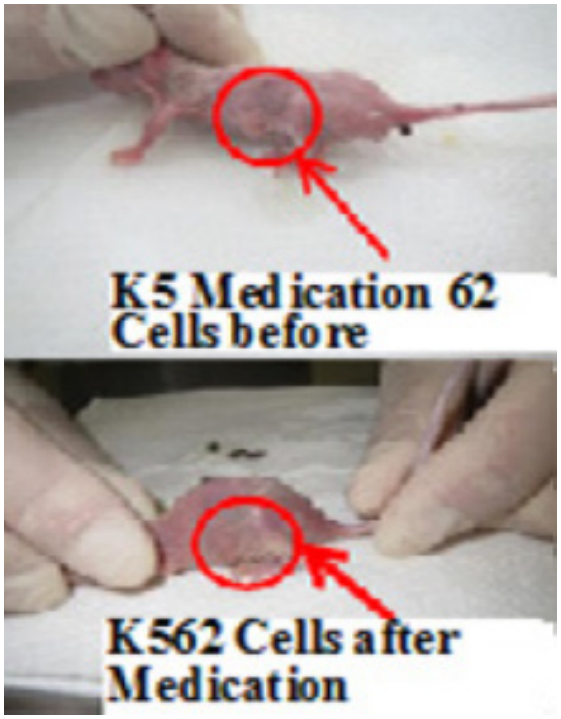


**Figure 3:** *In vivo* evaluation for TBMPP