

## NEW TRIVALENT LIGANDS OF THE ASGP-RECEPTOR

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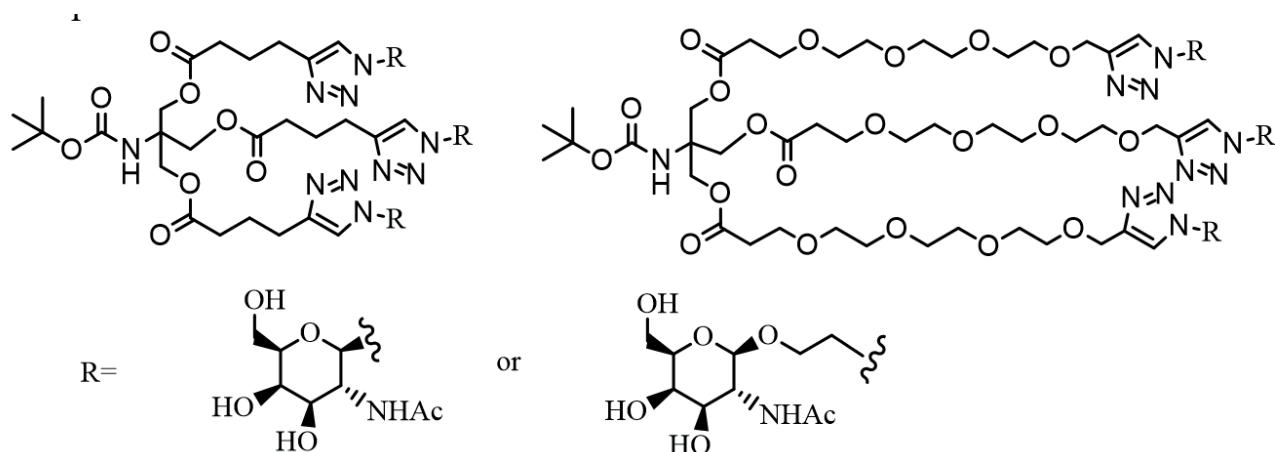
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In the treatment of liver diseases for targeted delivery of drugs to hepatocytes, the promising target is the asialoglycoprotein receptor (ASGP-R), which selectively recognizes monosaccharide derivatives, in particular, *N*-acetyl-*D*-galactosamine residues (GalNAc)<sup>1</sup>. Numerous multivalent ligands have been developed for the low molecular weight conjugates of ASGP-R, however, the multistage and high cost of synthesis limits their use in medical practice. Therefore, the actual scientific problem is the development and production of new multivalent ASGP-R ligands using modern and effective methods of organic chemistry.

At present work, the esterification of tris(hydroxymethyl)aminomethane with two different acids with terminal acetylene groups was originally carried out. Subsequently, the resulting products were introduced into the CuAAC-reaction with the azido-derivatives of GalNAc. As a result, new trivalent ligands of ASGP-R were synthesized with terminal *N*-acetyl-*D*-galactosamine residues.

The biological activity assays of the ligands showed their low cytotoxicity *in vitro*. The results of molecular docking revealed a high affinity to the carbohydrate-recognizing domain of ASGP-R. Evaluation of K<sub>d</sub> values to ASGP-R by the SPR-spectroscopy showed high binding potency of new ligands to the receptor.



## References

1. Maklakova S. Y. et al. Russian Chemical Bulletin, 2015, 64, 7.

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