Editorial

iMedPub Journals
www.imedpub.com

Archives in Chemical Research
ISSN 2572-4657

2021
Vol.5 No.1:21

Rationale for Chemical Modification

Alemayehu Gela*

Department of Zoological Sciences, Addis Ababa University, Addis Ababa, Ethiopia

Received: October 11, 2021; **Accepted:** October 18, 2021; **Published:** October 25, 2021

***Corresponding author:** Alemayehu Gela

alemaygb@yahoo.com

Department of Zoological Sciences, Addis Ababa University, Addis Ababa, Ethiopia

Citation: Gela A (2021) Rationale for Chemical Modification. Arch Chem Res. Vol.5 No.1:21

Editorial

Most siRNAs used in research today are made by chemical synthesis using phosphoramidite building blocks as single-stranded oligonucleotides and are annealed into double-stranded form. This approach permits incorporation of a good sort of natural and artificial modifications into the siRNA which will help solve a number of the issues related to administration of synthetic nucleic acids into cells or animals. Some problems that can be addressed using chemical modification include: Susceptibility to nuclease degradation. Activation of the innate immune system (OTE). Unwanted participation in miRNA pathways (OTE). Cell uptake and pharmacokinetics. The precise choice of chemical modifications to use can vary with the planning of the siRNA used, specific sequence, intended application, and method of delivery.

Most siRNAs used today for in vivo research applications are synthetic 21-mer RNA duplexes that mimic the planning of natural siRNAs. Similarly, 21-mer siRNAs are currently the lead compounds for variety of clinical and preclinical RNAi drug development programs. Alternative designs also are in use for both research and drug development, including blunt 19-mers, and asymmetric 25/27-mers or 27/29-mers. Some of these compounds directly load into RISC whereas others are substrates for Dicer and are processed into shorter species before RISC loading. The precise design of the siRNA employed can influence the selection or pattern of chemical modifications suitable to be used. Site selection is critical to the performance of siRNA compounds and an outsized amount of labor from many various groups has led to the event of fantastic site selection and design criteria also as computer assisted algorithms that facilitate this process. These design rules and algorithms were all developed using data from studies performed using unmodified siRNAs.

It is important to notice that the utilization of chemical modifications can alter the potency of a siRNA and regularly a chemically modified siRNA will show lower potency than the unmodified RNA version of that very same sequence, especially when extensively modified. Specifically, certain modification patterns are demonstrated to impair the power of an RNA sequence to trigger an RNAi effect whereas other patterns have less of an impact on potency. These effects vary with sequence, such that a given modification pattern can be effective at one site yet reduce potency of a siRNA at a second site. Thus empiric testing is usually necessary to ensure that a modified siRNA is effective when a known potent unmodified siRNA is converted to a modified form. Alternatively, initial site screenings are often done using only modified duplexes, bypassing use of unmodified RNA entirely. Design rules and site selection criteria specific for modified siRNAs haven't been reported.

Although it is possible to employ unmodified RNA duplexes to trigger RNAi responses in vivo, the use of chemical modifications can improve nuclease stability; reduce the risk of activating the innate immune system and decrease OTEs. Modifications also can be wont to facilitate delivery, improve bio distribution and increase plasma circulation half-life.