Effects of alkyl chain length and degree of unsaturation at the α-anomeric position of D-galactose on gel formation and small molecule solubility

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Narrative

1. Goals and Objectives

The main goal of this project is to first synthesize several carbohydrate based amphiphilic (bi-polar) molecules with varied chain length and degree of unsaturation in their nonpolar tail group. Second, and most importantly, these molecules will be used to investigate the effects of variability in the chain length and degree of unsaturation on their ability to form gel structures in various solvents as well as their ability to dissolve biologically and medically relevant molecules. To meet this end various preliminary steps will be undertaken. These steps include the synthesis of D-galactose derivatives with variable alkyl groups at the α-anomeric carbon, observation of the gelation capacity of these molecules in solvents ranging from extremely polar to nonpolar, and finally observation of the solubility potential of biologically and medically relevant molecules in the obtained gels.

To sufficiently meet the needs of the experiment a minimum of 8-10 different galactose analogs must be synthesized. Half of these molecules will be used to test the effects of alkyl chain length on the properties of the molecule and the other half will be used to test the effects of varied degrees of unsaturation. Furthermore, optimal characterization methods for the synthesized molecules and the gels will be elucidated over the course of the experiment by trial and error based on the methods reported in the literature and the means provided by the SVSU Chemistry Department.

If synthesis and characterization of the molecules run smoothly, our hypothesis is that there should be some observed correlation between adjustments of the aforementioned variables on not only solvent capacity but also gel formation and viscosity.

2. Background and Context

Low molecular weight (LMW) organogelators have attracted a considerable amount of attention in recent decades. These molecules are able to aggregate in organic solvents or water to form supramolecular structures that increase the surface tension of the solvent resulting in solvent immobilization and gel formation. These gels have displayed properties that are quite promising in various applications including topical or oral drug delivery, tissue engineering, and protein immobilization (Hari P.R. Mangunuru, 2015).

There are two basic types of LMW organogels that may be formulated; solid-matrix and fluid-matrix. Solid-matrix gels, much like the name suggests, form

supramolecular structures akin to those of a true solid. The molecules form rigid bonds in long polymeric chains, however due to their surrounding environment true crystalline structure is not achieved. These are the most abundantly utilized and understood organogellators (Anda Vintiloiu, 2008). Fluid-matrix gels, on the other hand, are formed when the gelating molecules aggregate into clusters known as micelles which then aggregate further. Micelles are a result of polarity effects between the molecules and the solvent. Micellation is only achieved when an amphiphilic solvent is placed into a polar or nonpolar solvent. For example, if water is introduced to an amphiphilic molecule the nonpolar regions will tend to cluster together in order to limit the amount of interaction with the polar solvent while the polar groups of the molecule will seek maximum exposure to the solvent. This interaction drives the formulation of spheres with the exterior being composed of polar groups and the interior being composed of nonpolar groups. This sphere is a micelle. After their formation micelles are able to interact with each other and form loosely bound bonds. These bonds are easily broken and reformed, giving the overall structure fluidity (Anda Vintiloiu, 2008). The LMW organogelators discussed of interest form fluid-matrix gels.

While there is a significant body of literature describing organogels, their makeup, and their applications, carbohydrate based gelators are relatively under reported in the literature. This could be due to the fact that other molecules (e.g. fatty acids) are just more obvious for use as a gelator in that they exist in nature as having an amphiphilic structure. Many carbohydrates on the other hand require some amount of modification to produce a molecular structure that can be useful for producing gels.

While many of the possible hypotheses surrounding organogelators have been tested using more common molecules there is still much to be elucidated about the properties and potential of carbohydrate based organogelators. For example, a paper published in 1964 synthesized glucose based micelle forming molecules and attempted to test for a relationship between alkyl chain length and the overall alkylation abilities of the molecules (Hutchinson, 1964). Their results were largely inconclusive and have yet to be sufficiently investigated. Furthermore, the effects of alkyl chain length and degree of unsaturation on the properties of a gel have been tested using lecithin, a fatty acid. However, the report was somewhat inconclusive and therefore leaves much more to be done to obtain more useful results (Rajiv Kumar, 2005).

3. Significance and Impact

It is difficult to deny the importance of nearly any scientific research in that, at the very least, it will add to the greater body of knowledge for someone else to utilize in future efforts. That aside, the project at hand will provide relevant information in an area of a field yet to be heavily researched. Furthermore, the potential real world applications of the knowledge to be gained from this project are relatively significant, especially in the way of pharmaceuticals.

As stated before, there is very little known about the usefulness, applications, and properties of carbohydrate based organogelators. There is a real possibility for untapped potential in this area. Perhaps the most promising aspect of these molecules is that carbohydrates are widely abundant in the natural world, and the simple carbohydrates to be utilized here are even more abundant. This means that any application utilizing these molecules will be able to be carried out for a relatively low cost. This is a factor that can often make or break a scientific pursuit.

One main application of organogels is pharmaceutical drug dissemination. Organogels are found in most topical creams and even in some medications administered orally or rectally. The micellar properties of fluid-matrix gels allow for the dissolution of some molecules that would not regularly dissolve in the surrounding solvent. This fact is particularly of interest in drug application because the inner- and intracellular environments throughout the body are varied. The gel, loaded with a specific drug, may be able to cross a threshold that the drug would not otherwise be able to cross on its own to get to the desired area. This project will attempt to find trends between small molecule solubility and various alkyl chain properties. Thus, providing further evidence either for or against carbohydrate organogelators as useful drug applicators.

As for myself, this project is extremely exciting. This is truly the purest scientific undertaking that I have attempted yet, in that I have come up with the question I would like to answer on my own, with guidance from Dr. Chaytor, and I will get to see it through to completion. Furthermore, this project will become my honors thesis next year, making it the culmination of my academic experience here at Saginaw Valley. If I could positively impact the scientific community with whatever results I obtain I feel that my goals as an undergraduate would be truly fulfilled.

I feel as though I am well suited to undertake a project such as this. During the summer of 2015 I held a research internship with the Saginaw Bay Environmental Science Institute. During my time there I worked with a team comprised of two high school students, a high school teacher, and Dr. Chaytor on a project which involved the chemical modification of the carbohydrate cellulose. During my time I gained a rich understanding of the importance of collaboration, proper laboratory proceedings, and problem solving. Furthermore, I hold a current position working in Dr. Chaytor's laboratory synthesizing novel cyclic peptides and analyzing them for their biological relevance in reducing bone density loss. I strive to continue to further my scientific knowledge, laboratory aptitude and use my developing knowledge and skills to solve a new problem.

4. Timeline

May	Obtain necessary materials
Jun-Aug	Begin synthesis of D-galactose derivatives, characterize synthesized molecules
Sept-Oct	Begin gel formation testing, continue synthesis, continue characterization
Nov-Dec	Begin solubility testing, continue gel formation testing, complete final syntheses and characterization
Jan-Feb	Complete solubility testing, begin writing thesis
Mar	Complete thesis, present at ACS national meeting
Apr	Defend honors thesis, submit final report

5. Evaluation

If I am able to keep on pace with the timeline that I have described above, then I will know that as far as proceeding through the project I am doing well. As for results, if I am able properly characterize all of the compounds that I synthesize and their characterizations are in line with what was expected then the experiment will be a success; I will be able to use these compounds for effective assessment of their properties and therefore obtain useful results. Throughout the process I will continue to regularly meet with Dr. Chaytor to ensure that the timeline is being met and for any sort of troubleshooting needs.

After the project has finished the information will be disseminated mainly in the form of talks and poster presentations. I will assuredly be defending this research as my honors thesis in the form of a talk. I plan to present at the ACS national meeting in San Francisco, the SVSU SET symposium, and UGRP symposium as well. There will likely be more opportunities for other oral or poster presentations and possible publication in the Journal of Undergraduate Research or other peer-reviewed journals.

References

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