Photophysical Studies of 9-aminoacridine Derivatives

Arec Phanthapanya, Arinzechukwu Aniekwe, Sokhna Ndiaye, Tyler Sawyer, Neville Forlemu, Ajay Mallia

Georgia Gwinnett College, Lawrenceville, GA

Abstract

Acridine is a known DNA intercalating scaffold that is used for anti-cancer and anti-bacterial agents. N-(acridin-9-yl)alkanamides have been synthesized with dodecyl (9-A12), tetradecyl (9-A14), and octadecyl (9-A18) carbon chains to study the photophysical properties using UV-Vis and fluorescence spectroscopy. 3ß-cholesteryl N-(9-acridinyl) carbomate (9-AC) was also prepared and studied as well. It is believed that the acylation of 9-aminoacridine with these hydrophobic tails and their lengths affects the binding with DNA. The analysis showed an increase in molar absorptivity as the length of the chain increased with values of 1466, 1431, 4972, and 8100 L mol-1 cm-1 for 9-A12, 9-A14, 9-A18, and 9-AC respectively.

Introduction

- **9-aminoacridine is a pharmaceutically active fluorescent compound.**
- **Acridines bind noncovalently to DNA which enables a reversible process.**
- **Acridine derivatives are used as pH sensitive fluorescent molecular probes due to their small size and high quantum yield of emission.**
- **Short hydrophobic tails exhibit less sensitivity to biological micro-environments while long hydrophobic tails show enhanced fluorescent activity.**

Present work and designing strategy

- **The objective of this experiment is to observe the photophysical properties of the 9-aminoacridine derivatives**

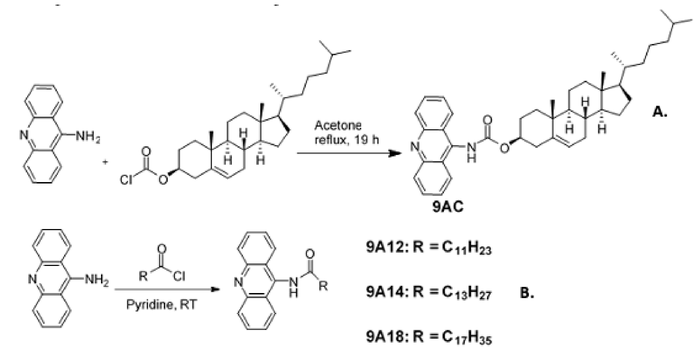

Figure 1. Scheme of Acridine Derivatives: **A.** 9AC and **B.** 9A12, 9A14, and 9A18

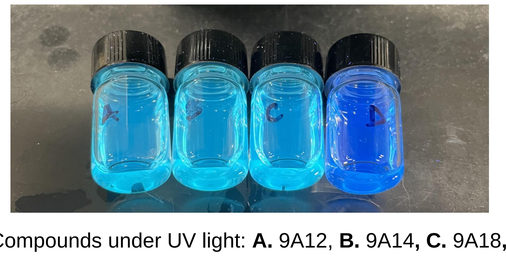

Figure 2. Compounds under UV light: **A.** 9A12, **B.** 9A14**, C.** 9A18**, D.** 9AC

Methods

- **9-aminoacridine hydrochloride (5.9 g) was mixed in distilled water (60 mL) and was heated to 90°C, and stirred for 15 min until completely dissolved. NaOH (8.4 g) was added to the solution, stirred for 15 mins, and was cooled to RT.**
- **The precipitate (9-aminoacridine, 9-AA) was then vacuum filtered, washed with distilled water and ethanol, and allowed to dry under a lamp.**
- **To synthesize a 9-AA derivative, the same steps previously stated can be used. Instead of distilled water, use Pyridine. The reaction also takes place at RT. For 9-A12, replace NaOH with myristoyl chloride. For 9-A14, replace NaOH with lauroyl chloride. For 9-A18, replace NaOH with steroyl chloride.Each derivative was then vacuum filtered, washed with distilled water and ethanol, and allowed to dry under a lamp.**
- **To synthesize 9-AC, 500 mg of 9-AA was added to a 500 mL round bottom flask. 250 mL of Acetone was added to the round bottom flask, heated to 60°C, and stirred until 9-AA dissolved. Cholesteryl chloroformate (1:1 eq) was added to saturated with 10 mL of acetone and added to the solution dropwise.**
- **The solution was then allowed to reflux for approximately 19 hours at 45°C.The precipitate (9-AC) was then vacuum filtered, washed with distilled water and ethanol, and allowed to dry under a lamp.Each derivative was characterized using IR Spectrophotometry, TLC (1:1 hexane/ethyl acetate), and melting point.**
- **A stock solution of each sample was prepared at 1 mM with DMSO as the solvent and then a diluted solution of 0.1 m M was prepared for each sample for UV-Vis analysis on a Perkin Elmer PDA UV/VIS Lambda 265 Spectrophotometer.**
- **Each sample was purified and recrystallized using Ethanol and Distilled Water for photophysical studies**

Results and discussion

Using 9-aminoacridine as a base, a peak was observed at 409 nm under UV-Vis spectroscopy. Each subsequent acridine derivative all indicated a peak within 409±4 nm. The absorption value of each peak was recorded and the molar extinction coefficient (ε), or molar absorptivity, was calculated using the Beer-Lambert Law with the cuvette having a pathlength of 1 cm.

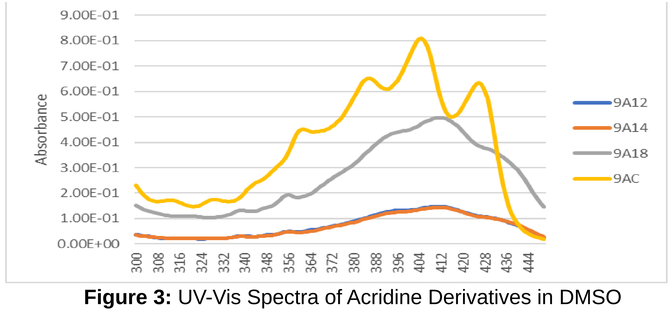

Figure 3: UV-Vis Spectra of Acridine Derivatives in DMSO

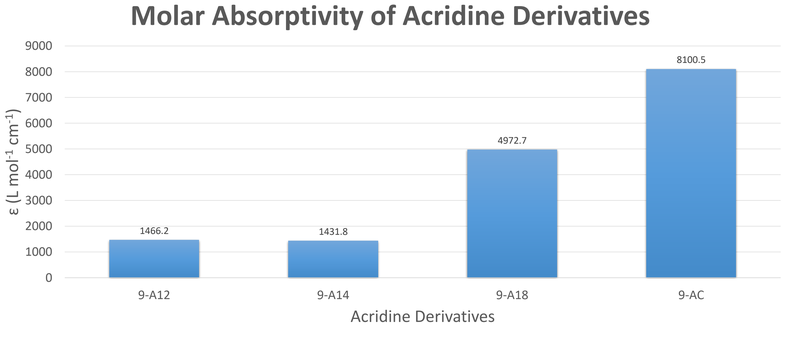

Figure 4: Molar Absorptivity values of Acridine Derivatives

Results and discussion

With the absorbance, it can be observed that 9AC absorbs more light than the alkanamides and a positive trend can also be observed as the length of the carbon chain increases. With these longer, hydrophobic tails, more fluorescent activity is taking place. It is stated that this activity relates to the binding of DNA. It can be assumed that 9AC, being cholesterol based and having the longest carbon chain, will have the higher affinity to DNA compared to the other compounds.

Each compound was purified and recrystallized using Ethanol. 9-A12 and 9-A14 showcased a clear, needle-like crystalline structure. Unfortunately, 9-A18 and 9-AC did not achieve desirable results after several attempts of recrystallization. Recrystallization with other solvents such as Methanol and Ethyl-Acetate were also attempted but also failed to produce results.

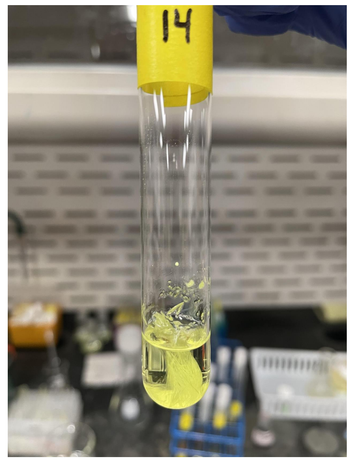

Figure 5: Crystal formation of 9A14

Conclusions

Computational docking studies conducted in previous research indicated that 9-AC binds strongly to DNA when compared to the N-(acridin-9-yl)alkanamides. The research conducted in the present study suggests that 9-AC with its higher molar absorptivity would exhibit the most fluorescent activity among the N-(acridin-9-yl)alkanamides and confirms the computational docking studies. A positive trend can be observed in the molar absorptivity of each compound as the length of the carbon chain increases. Once the equipment for fluorescent spectroscopy is ready, more data can be extracted to further strengthen that idea.

References

- SALEM, O.; VILKOVA, M.; PLSIKOVA, J.; GROLMUSOVA, A.; BURIKOVA, M.; PROKAIOVA, M.; PAULIKOVA, H.; IMRICH, J.; KOZURKOVA, M. DNA Binding, Anti-Tumour Activity And Reactivity Toward Cell Thiols Of Acridin-9-Ylalkenoic Derivatives. *Journal of Chemical Sciences* 2015, *127* (5), 931-940.
- Alok, K. Interaction Of Fatty Acid-Containing 9-Aminoacridine Derivative With Surfactants And Bio-Surfactants: Synthesis And Photophysical Studies. *Journal of Photochemistry and Photobiology A: Chemistry* 2018, *367*, 321-326.
- Tripathi, A. Binding Interaction Of N-Acetylated Acridine Conjugate With Ct-DNA And B-Cyclodextrin: Synthesis And Photophysical Studies. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* 2018, *205*, 497-502.

Acknowledgments

The authors would like to give thanks to the School of Science and Technology of Georgia Gwinnett College for funding and the opportunity to conduct this research.