PAMAM Dendrimer in Acne Vulgaris Treatment

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Abstract

Dendrimers are nano-sized synthetic polymers of repeated branching chains extending radially from the core. The outermost surface is often characterized by functional groups or reactive molecules that can chemically interact with other molecules of interest. Because of their unique properties, dendrimers are used and studied for various applications. The G2 polyamidoamine dendrimer (PAMAM-NH_2) possesses the ability to interact with bacterial membranes and has shown potential for target specificity. Our research aims to study the PAMAM dendrimer as a potential antimicrobial in treating the chronic skin disorder Acne vulgaris. This project aims to elucidate better the PAMAM dendrimer's nature regarding its antimicrobial activity, the dose dependency of its efficacy, its target specificity, its relationship with antibiotic resistance, and its interaction with collective skin commensals. This project studies the antimicrobial effect of the G2 PAMAM dendrimer on the bacterial species *Cutibacterium acnes and Staphylococcus epidermidis.*

Introduction

Acne vulgaris is a chronic skin disorder that involves the bacterial infection of hair follicles and sebaceous glands. Acne is caused by multiple factors involved in the microbiome of the skin. Among the skin commensals, *Cutibacterium* (*C. acnes*) has been shown to be the main bacteria involved in acne development and inflammation. Therefore, antibiotics that target *C. acnes* have been the primary treatment for acne for the past four decades. Heavy reliance on antibiotics, including oral and topical macrolides and clindamycin, has dramatically increased the rates of resistance to these antibiotics in the last two decades. The goal of current acne treatment is to shift away from antibiotic treatments, which purge the skin microbiome and induce resistance, to treatments that can specifically target *C. acnes*, not upset the balance of the microbiome, and not induce resistance.

Dendrimers have been shown to possess antimicrobial properties. This ability is attributed to positively charged functional groups which puncture the negatively charged bacterial membrane. Furthermore, dendrimers have been shown to target specific strains within bacterial species. These preferences are based on the differences in charge affinity between the dendrimer and bacterial membrane. Therefore, dendrimers with positively charged functional groups, such as the PAMAM G2 dendrimer, can be tested for differences in affinity to certain bacteria and bacterial strains. In addition to their target specificity, dendrimers have been proven not to induce resistance in bacteria.

Results

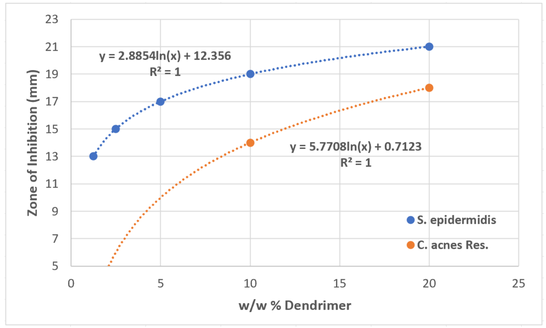


Figure 1: The zones of inhibition plotted against the w/w % PAMAM dendrimer with 0.9 % saline as the solvent.

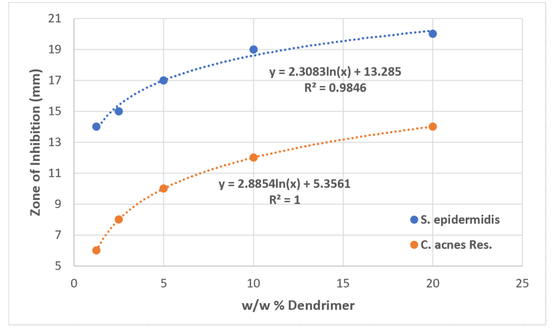
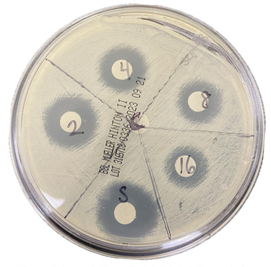


Figure 2: The zones of inhibition plotted against the w/w % PAMAM dendrimer with pH 5 Buffer solution as the solvent.

***C. acnes Res.* + PAMAM Dendrimer in pH 5 Buffer solution**

***C. acnes* + *S. epidermidis* + PAMAM Dendrimer in 0.9 % saline solution**



***S. epidermidis* + PAMAM Dendrimer in pH 5 Buffer solution**

***S. epidermidis* + PAMAM Dendrimer in 0.9 % saline solution**

	S. epidermidis (mm)	C. acnes W.T. (mm)	C. acnes Res. (mm)
Control (0.9 % saline)	0	0	0
Stock	21	10	18
1:2	19	0	14
1:4	17	0	
1:8	15	0	
1:16	13	0	

Table 1: The zones of inhibition of *S. epidermidis*, *C. acnes*, and Clindamycin-resistant *C. acnes* resulting from the 20 w/w % PAMAM dendrimer in 0.9 % saline solution.

	S. epidermidis (mm)	C. acnes W.T. (mm)	C. acnes Res. (mm)
Control (pH 5 Buffer)	0	0	0
Stock	20	0	14 (P.I.)
1:2	19	0	12 (P.I.)
1:4	17	0	10 (P.I.)
1:8	15	0	8 (P.I.)
1:16	14	0	6 (P.I.)

Table 2: The zones of inhibition and partial inhibition (P.I.) of *S. epidermidis*, *C. acnes*, and Clindamycin-resistant *C. acnes* resulting from the 20 w/w % PAMAM dendrimer in the pH 5 Buffer solution.

Conclusions and Future Work

- The most effective dendrimer concentration was the 20 w/w % dendrimer solution with 0.9 % saline as the solvent. The dendrimer was more effective against *S. epidermidis* than *C. acnes.*
- The relationship between the concentration of dendrimer and the zone of inhibition shows a logarithmic relationship.
- The pH 5 Buffer and the 0.9 % saline solvent did not show significant differences in efficacy towards either the *C. acnes and S. epidermidis*. Future research would include testing varying pH buffer solutions above and below the pH of the skin.
- The dendrimer significantly affected the clindamycin-resistant strains of both *C. acnes* and S. *epidermidis*. When *C. acnes* and *S. epidermidis* develop resistance to clindamycin, they become more susceptible to the PAMAM dendrimer. Therefore, further studies of the PAMAM dendrimer in treating Acne vulgaris should focus on combining antibiotics and dendrimers for future treatment regimens. Furthermore, the PAMAM dendrimer treatment may be most effective for cases of Acne with antibiotic resistance.
- The *C. acnes* grew more aggressively than the *S. epidermidis* when grown on the same plate. The *C. acnes* inhibited the growth of the *S. epidermidis* significantly.

Methodology

A series of Kirby-Bauer disk diffusion tests were performed to test the interaction of *C. acnes* and *S. epidermidis* with the G2-Hex-NH_2 PAMAM dendrimer. The *C. acnes* and *S. epidermidis* were grown on Mueller Hinton agar and streaked in three planes to ensure even distribution along the surface of the agar. A pipette was used to administer and infuse the dendrimer solutions into filter paper disks. A control disk was made for each diffusion test and placed in the center of the plate. Four parameters were tested:

- **Concentration:** A 20 w/w % dendrimer stock solution was made in two different solvents. Five concentrations were made via a two-fold serial dilution.
- **Solvent:** A 0.9 % sterile saline solution and a pH five phosphate buffer solution (To mimic the skin's pH) were made. The buffer solution was sterilized by filtration through a 0.22 µm syringe filter.
- **The effect of antibiotic resistance on dendrimer efficacy:** Resistance to clindamycin (antibiotic) was induced in *C. acnes* and *S. epidermidis*. The antibiotic-resistant strains were tested against the dendrimer.
- **The effect of bacterial synergy on dendrimer efficacy:** A double-plate was made containing both *C. acnes* and *S. epidermidis* (To mimic the effect of the microbiota). The double-plate was tested against the dendrimer.

The "zone of inhibition" is an indirect measurement of the ability of that antimicrobial to inhibit that bacteria *in vivo*. The Clinical Laboratory Standards Institute (CLSI) publication of the Performance Standards for Antimicrobial Disk Susceptibility Tests represents the standard for clinical laboratories performing the test. Because the G2 dendrimer is a novel antimicrobial, there are no official standards to compare the results from the test. Therefore, the Kirby-Bauer disk test results will not correlate to *in vivo* antimicrobial susceptibility.

Literature Cited

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