

Antibacterial Activity of Clindamycin/BPO in Combination With Adapalene

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SYNOPSIS AND OBJECTIVE

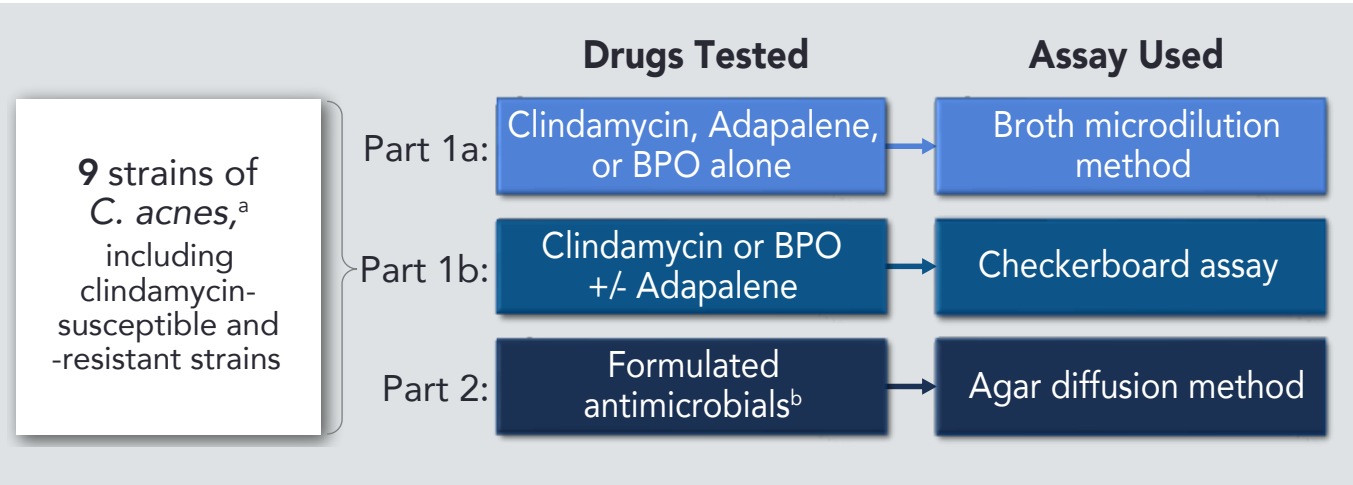
- Acne treatment guidelines recommend the addition of the antimicrobial benzoyl peroxide (BPO) when long-term topical antibiotic use is necessary, to reduce the risk of antibiotic resistance in *Cutibacterium acnes* (*C. acnes*)¹
- Pairing the antibiotic/BPO combination with a retinoid, such as adapalene, may further increase treatment efficacy^{2,3}
 - Adapalene targets acne pathogenesis by modulating cellular proliferation, differentiation, and keratinization^{4,5}
- However, as research on adapalene's antibacterial activity is limited,⁶ it is not known if adapalene can improve the antimicrobial activity of antibiotics and BPO
- To determine if adapalene improves antimicrobial activity, this in vitro study evaluated the susceptibility of *C. acnes* isolates to clindamycin, adapalene, and BPO alone or in combination (Figure 1)

METHODS AND RESULTS

Part 1a: *C. acnes* Susceptibility to Clindamycin, Adapalene, and BPO

- The susceptibility of 6 acne-associated *C. acnes* strains was assessed via minimum inhibitory concentration (MIC) values obtained from the broth microdilution method (Figure 2, left)

FIGURE 1. Study Overview



^aIncluding 8 acne-associated strains and 1 neutral strain that is sometimes classified as acne-associated. Classification based on Fitz-Gibbon S, et al.⁷
^bCLIN 1.2%/adapalene 0.15%/BPO 3.1% gel (Ortho Dermatologics), Clindamycin 1% gel (Ortho Dermatologics), CLIN 1.2%/BPO 3.75% gel (Ortho Dermatologics), BPO 5%/erythromycin 3% gel (Ortho Dermatologics), BPO 3% gel (Ichthyo-Gesellschaft), adapalene 0.1% gel (Galderma laboratories).
BPO, benzoyl peroxide; CLIN, clindamycin phosphate.

- Clindamycin demonstrated low MIC values against some strains and high values against others; BPO and adapalene demonstrated high MIC values (Figure 2, right)

Part 1b: Effect of Adapalene + Clindamycin or BPO on *C. acnes* Inhibition

- The effect of combining adapalene with clindamycin or BPO on *C. acnes* inhibition was evaluated using a checkerboard assay, wherein 2 test compounds are combined in varying concentrations (Figure 3, left)
- The combination of adapalene and clindamycin had an additive effect for 3 out of 4 acne-associated strains tested and no interaction for 1 strain (Figure 3, right)
 - This additive effect was maintained when the experiment was repeated in the presence of sebum (data not shown)

Part 2: *C. acnes* Susceptibility to Antibiotic Formulations

- *C. acnes* susceptibility to single or combination formulations was determined by measuring the antibacterial zone of inhibition using agar diffusion method (Figure 4, left)
- Activity of single formulations varied against the 8 acne-associated *C. acnes* strains tested, whereas fixed-dose combination formulations had generally similar activity against the strains (Figure 4, right)

Study Limitations

- Limitations of this in vitro study are detailed in Figure 5

FIGURE 2. *C. acnes* Susceptibility to Clindamycin, Adapalene, and BPO (Part 1a)

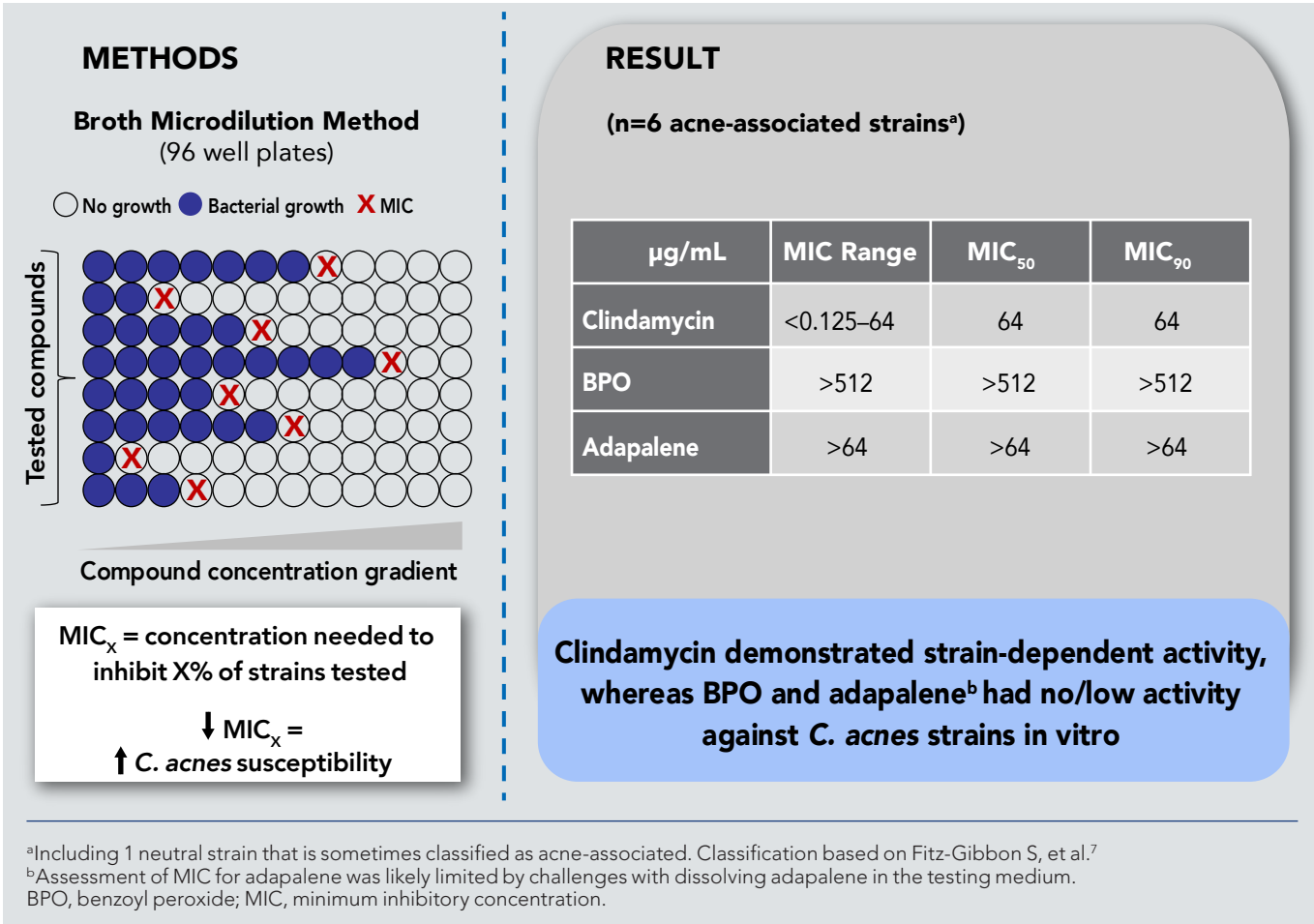


FIGURE 3. Effect of Adapalene + Clindamycin or BPO on *C. acnes* Inhibition (Part 1b)

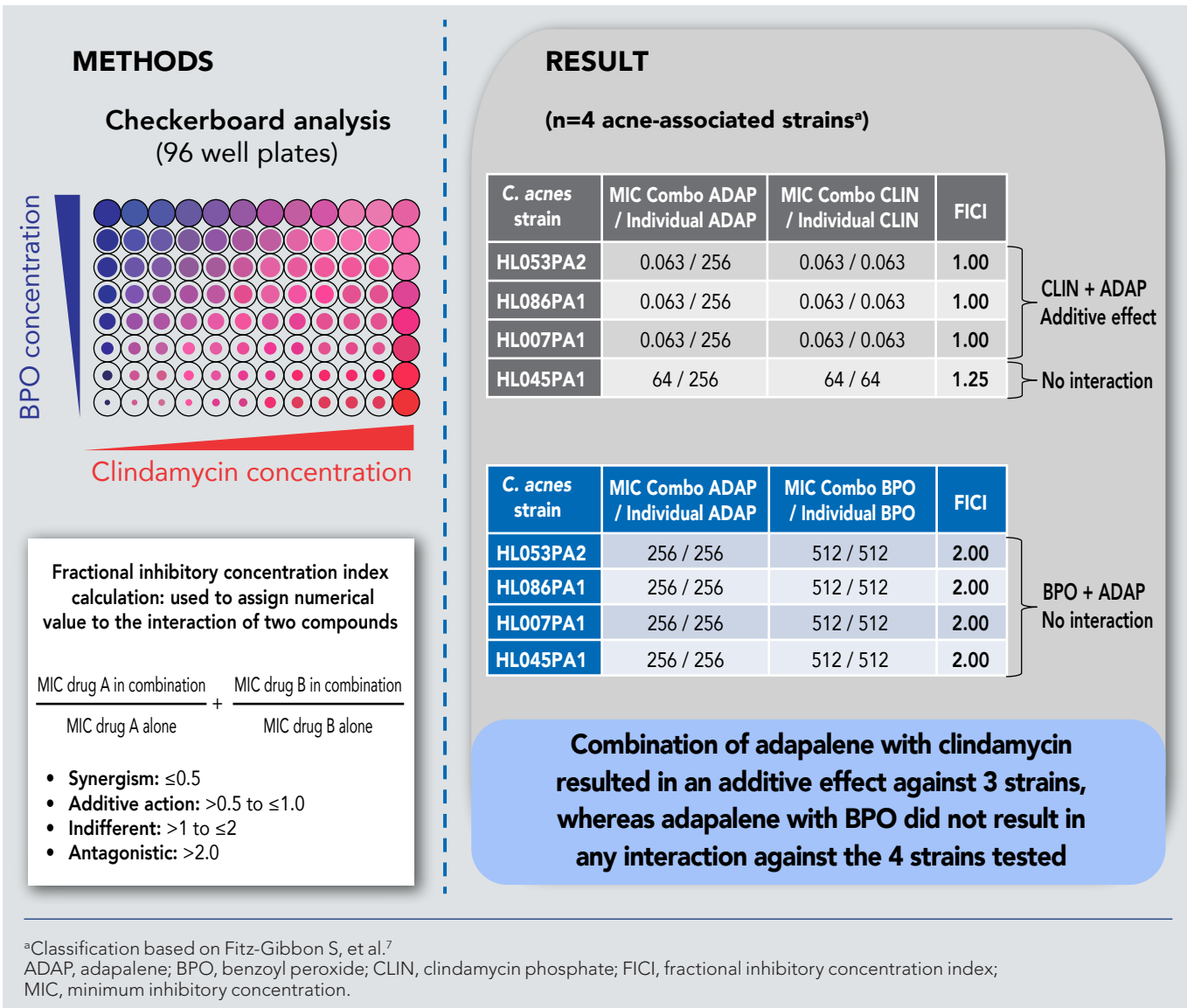


FIGURE 4. *C. acnes* Susceptibility to Antibiotic Formulations (Part 2)

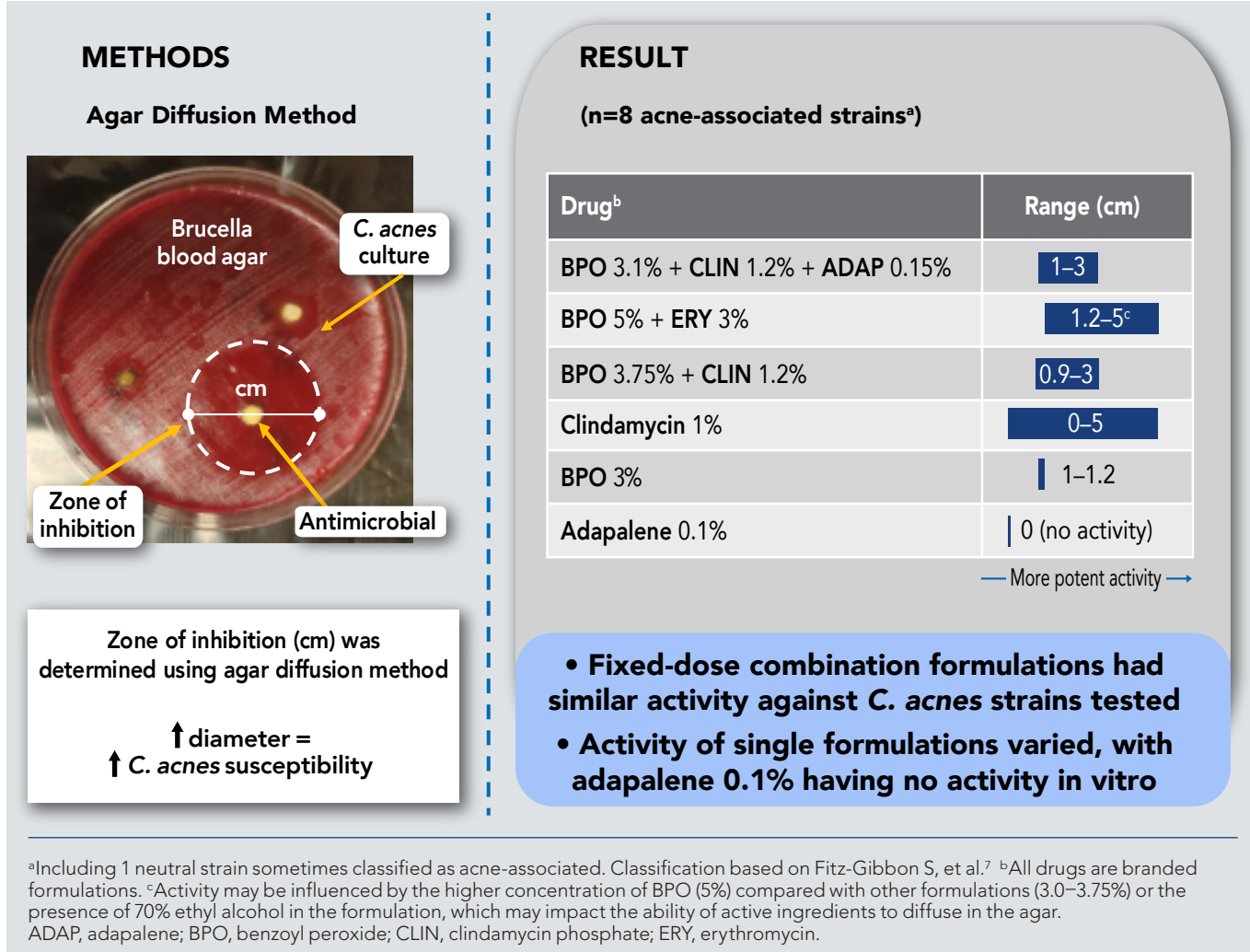
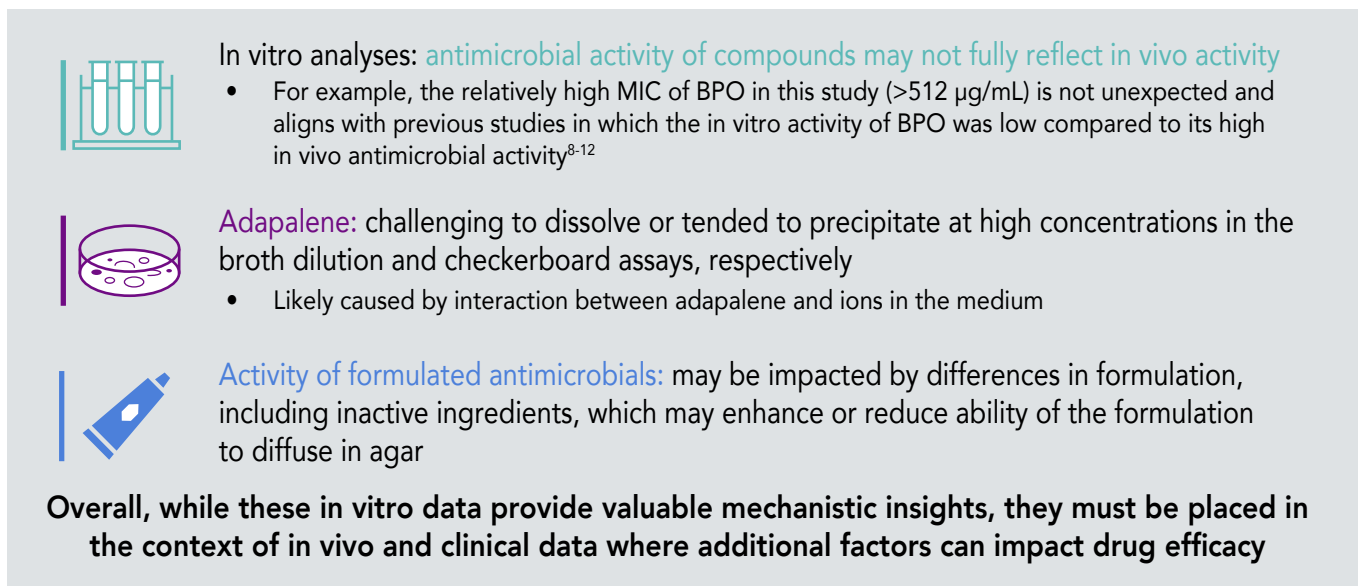


FIGURE 5. Study Limitations



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CONCLUSIONS

- Clindamycin demonstrated strain-dependent activity against *C. acnes* in vitro, as expected for an antibiotic
- Adapalene had an additive effect on the antimicrobial activity of clindamycin against 3 out of 4 *C. acnes* strains tested, but no effect on BPO activity in vitro
- These data suggest that when combined with clindamycin/BPO, adapalene may enhance clindamycin's antimicrobial activity, while also bringing its own, unique retinoid mechanism of action to the triple combination
 - This triple combination may further benefit from the ability of BPO to enhance clindamycin's antimicrobial activity¹³
 - This is corroborated by a meta-analysis in which the combination of an antibiotic, retinoid, and BPO was among the top 2 most efficacious of all treatments for acne¹⁴

AUTHOR DISCLOSURES

Mahmoud Ghannoum has acted as a consultant or received contracts from Scynexis, Inc, Bausch & Lomb, Pfizer, and Mycovia. James Q. Del Rosso has served as a consultant, investigator, and/or speaker for Ortho Dermatologics, AbbVie, Almirall, Amgen, Arcutis, Biofrontera, Cassiopea, Cutera, Dermavant, EPI Health, Evomune, Galderma, Incyte, JEM Health, Journey, La Roche-Posay, LEO Pharma, Lilly, L'Oreal, MC2 Therapeutics, Novan, Nutrafol, Pfizer, Sente, Strata, Sun Pharma, UCB, and Wyne. Linda Stein Gold has served as investigator/consultant or speaker for Ortho Dermatologics, LEO Pharma, Dermavant, Incyte, Novartis, AbbVie, Pfizer, Sun Pharma, UCB, Arcutis, and Lilly. Leon H. Kircik has served as either a consultant, speaker, advisor, or investigator for Allergan, Almirall, Epi Health, Galderma, Novartis, Ortho Dermatologics, and Sun Pharma. Julie C. Harper has received honoraria from Almirall, Cutera, Galderma, LaRoche-Posay, Ortho Dermatologics, and Sun Pharma. Other authors have nothing to disclose.