

Topical antibiotics: Current options include clindamycin, clarithromycin, azithromycin, and nadifloxacin. Tetracycline and erythromycin are no longer easily available. Topically applied antibiotics work slowly and are marginally effective.^[1] They are rarely adequate as a monotherapy but are useful adjuncts to all forms of systemic and topical therapy. Their antibacterial, anti-inflammatory, and, possibly comedolytic effects^[2] are optimized through careful determination of concentrations, and their suitability is enhanced by making them available in different forms, for example, creams, gels, solutions, pledgets, and sachets to cater to diverse skin types and changing dynamics of the skin brought about by changes in weather conditions, physical activities, and effects of concomitant therapies. Gels are preferable as they offer the best combination of being nonoily, invisible, and having good percutaneous absorption. In our country, topical antibiotics are generic and the selection is overwhelming. The bioequivalence of various products has not been addressed and it is left to the prescribing dermatologist to make that judgement. Further, topical products are more vulnerable to 'shelf-conditions' and this too impacts efficacy. There is much more to prescribing topical antibiotics. They should be applied to the entire area, in a quantity that readily absorbs, ideally twice daily. They may be used in conjunction with other topical products (sunscreens, moisturizers, retinoids, antifungals) but only after ascertaining compatibility. Topical antibiotics should be discontinued if no therapeutic benefit is observed in 6–8 weeks.^[1] Resistance to topical antibiotics is frequent and extends to cross-resistance between commonly used antibiotics, especially tetracycline, erythromycin, and clindamycin.^[1] Indiscriminate use of topical antibiotics is a major cause of bacterial resistance and should be curbed.^[3] Other than occasional erythema, peeling, burning, itching, and dryness, topical antibiotics are well tolerated and safe.^[1] There are rare reports of pseudomembranous colitis from topical clindamycin.^[1] We are fortunate in India to have available newer topical antibiotics such as clarithromycin, azithromycin, and nadifloxacin. While clarithromycin and azithromycin, being macrolides, have quietly replaced erythromycin without much documentation, nadifloxacin is a brand new entrant and has been clinically evaluated in inflammatory acne.^[4] Nadifloxacin is a fluorinated

quinolone that inhibits DNA gyrase, and has strong antibacterial activity against Gram-negative and Gram-positive bacteria.^[4] In a double-blind study comparing nadifloxacin 1% cream with erythromycin 2% cream in acne vulgaris, the two formulations were found to be equally effective at 12 weeks (66.7% versus 64.7%, respectively); however it was noted that while the erythromycin cream was only effective against *P. acnes*, nadifloxacin cream lowered counts of coagulase negative staphylococci as well as *P. acnes*.^[5] Further, antibiotic resistance to nadifloxacin was extremely low compared to erythromycin.^[5] Several formulations of nadifloxacin are available in our country, including a gel. Lessons from *P. acnes* resistance to erythromycin should alert us to the possibility of the same happening with clarithromycin and azithromycin?

TOPICAL ANTIBIOTICS

- Clindamycin, clarithromycin, azithromycin, and nadifloxacin.
- Work slowly; marginally effective.
- Rarely adequate as monotherapy.
- Indiscriminate use results in antibiotic resistance.

Benzoyl peroxide: Benzoyl peroxide (BPO) is a safe and effective, time tested, agent in the treatment of acne.^[1] In India, it is readily available as 2.5%, 5%, and 10% gel, as a wash, and as a bar soap. BPO gel is more stable and allows better release of the active ingredient.^[1] Internationally, other concentrations (1–10%), and other formulations (cream, lotion, cleanser, soap) are available.^[1] It is an excellent choice in the treatment of mild and moderate acne.^[1] Its principal mode of action is antibacterial (possibly bactericidal?) and to a lesser extent as comedolytic.^[1] BPO is more effective than topical erythromycin and clindamycin.^[6] Combination of BPO and erythromycin or BPO and clindamycin is more effective than BPO alone and is less irritating.^[7,8] Topical BPO and BPO/erythromycin combination are deemed to be similar in efficacy to oral oxytetracycline and minocycline.^[9] BPO has the advantage that bacterial resistance does not develop.^[1] It can be used as monotherapy though it is more effective in combination (vide supra). It needs to be applied to the entire surface. It is better to initiate therapy at lower concentrations (2.5%) because there

is a potential for irritation. Whenever irritation is encountered it can be overcome by gradual induction of the therapy.^[5] Though used once daily generally, BPO may be applied twice daily.^[1] BPO tends to bleach hair, clothing, and bed-linen,^[10] and perilesional skin with spot treatment.

TOPICAL BENZOYL PEROXIDE

- Available as 2.5% and 5% gel, wash, bar soap.
- Antibacterial action.
- Safe, effective, time-tested, economical antiacne agent.
- Can be used as monotherapy.
- Used concomitantly, helps prevent resistance to antibiotics.

Topical metronidazole: In gel formulation, it is the first-line treatment for rosacea and is also useful in overlap cases – acne/rosacea, and acne treated with topical steroids (steroid rosacea) [Figures 57-58]. Its mode of action is antibacterial and anti-inflammatory. In straightforward acne patients, it was found to be no more effective than placebo.^[11]

Dapsone: Dapsone has previously been used as an oral adjunctive therapy for severe inflammatory acne. It has anti-inflammatory and antibacterial properties. Recently it has been possible to formulate it as 5% aqueous gel and it has been clinically evaluated in the USA.^[12] In two large randomized studies involving 3010 subjects, dapsone gel was compared with the vehicle gel over 12 weeks. Dapsone-treated patients achieved superior results in reducing both inflammatory and

noninflammatory lesions. The difference was apparent as early as two weeks. There were no systemic effects, and acne patients with G-6PD deficiency tolerated the dapsone gel. The studies concluded that dapsone 5% gel was effective, safe, and well-tolerated treatment for acne with rapid onset of action.^[12] Our limited experience with dapsone gel, for the short period it was available in the Indian market, was not as favorable.

Azelaic acid: It is a naturally occurring dicarboxylic acid produced by the yeast fungus *Pityrosporum ovale*. It has antibacterial and anticomedonal properties and is felt by some to be equal in efficacy to BPO or tretinoin.^[13,14] The efficacy of azelaic acid may be increased by using it in combination with other topical medications such as retinoids, antibiotics, or BPO. Another beneficial effect of this agent is to decrease hyperpigmentation caused by acne. Azelaic acid is available as 10% and 20% cream and is to be applied twice daily. It frequently causes transient burning and tingling sensation, and occasionally mild erythema and pruritus.

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Figure 57: (a and b) Steroid-treated acne showing a mixed picture of rosacea, seborrheic dermatitis, and acne. Note striae – also steroid induced



Figure 58: (a and b) Steroid-modified acne before and after treatment

- human peripheral blood mononuclear cells and normal human keratinocytes. *J Dermatol Sci* 2005;38:47-55.
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