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The two limbs of Dermatologic Drug Development: Seredipity and Systematic Drug Repurposing

Sidharth Sonthalia[1], Nripen Kachhawa[2], Mahima Agrawal[3]

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Author Affiliation:
[1]Editor-in-Chief, RFP Journal of Dermatology, Consultant Dermatologist & Dermatosurgeon at Skinnocence: The Skin Clinic, Gurugram, Haryana 122009, India & Member, World Medical Association (WMA). [2]Junior Resident & Clinical Assistant, Skin Clinic, MDM Hospital Campus, Jodhpur, Rajasthan 342003, India, [3]Senior Resident, Dept. of Dermatology & STD, Lady Hardinge Medical College & Associated Hospitals, New Delhi, Delhi 110001, India.

Corresponding Author:
Sidharth Sonthalia, Consultant Dermatologist & Dermatosurgeon at Skinnocence: The Skin Clinic, Gurugram, Haryana 122009, India.
E-mail: sidharth.sonthalia@gmail.com

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The term drug repurposing has recently soared up the popularity charts of medical academia. Veritably drug repurposing has, for decades served as the source of majority of drugs being used in cutaneous medicine whether inspired serendipitously [1] or effectuated through plausibility-backed systematic trials. Perfection of serendipitous discovery of a drug's positive side-effect on a skin abnormality when administered for a completely unrelated co-morbidity also called the Renbok phenomenon [2] constitutes the first limb of dermatologic drug development. This concept dates back to Kligman's chance discovery of anti-aging effects of topical tretinoin when given for facial acne [3] and is illustrated with the following examples: minoxidil and finasteride for alopecias stemming from their hair growth 'side effect' observed in patients who were administered the drugs for hypertension and benign prostate hyperplasia respectively [4,5]; vitamin D analogues for psoriasis following dramatic improvement in an old patient who was actually given oral vitamin D for osteoporosis [6]; low-dose tranexamic acid for melasma extrapolated from reduced hyperpigmentation discovered in a patient with chronic urticaria for which the plasmin inhibitor was given [7,8]; tofacitinib for alopecia areata whilst the janus kinase inhibitor was primarily tried to control the patient's refractory psoriasis [9,10]; and the legendary discovery of aesthetic indications of botulinum toxin (BoNT) by the medico-marital sorority of the Carruthers, when the forehead lines disappeared in a patient suffering from blepharospasm treated with BoNT by Dr. Jean, an ophthalmologist, whose dermatologist husband Dr. Alistair Carruther later explored the science underlying this observation [11]. Planned repurposing based on thorough research constitutes the other, albeit less appreciated and addressed limb of pharmaceutical development in dermatology: Immunomodulatory effects of DMARDs like methotrexate, cyclosporine, sulphasalazine and anti-TNF-α biologics used in rheumatoid arthritis for pathogenetically related skin conditions especially psoriasis; antimycotic ciclopirox olamine for multi-drug-resistant bacterial infections of the skin [12-14]; NK-1 inhibitor aprepitant typically used for prevention of chemotherapy-induced and postoperative nausea and vomiting in cancer patients repurposed for chronic refractory pruritus of diverse origins [15,16]; ornithine decarboxylase inhibitor (ODCI) anti-trypanosomal oral drug eflornithine hydrochloride repurposed topically for reducing unwanted hair growth, e.g. in hirsutism, and for prophylaxis against development of non-melanoma skin cancers (NMSCs) [17,18]; translating the repigmenting effect of UV light via induction of PGE2 production into clinical repurposing of PGE2 gel for treatment of vitiligo [19]; and cosmeceutical repurposing of melatonin in AGA using nanostructured lipid carriers [20] exemplify this approach.

However, the biggest concern in this area is the relative lack of evidence in favour of many seredipitiously discovered drugs. Thus, Dermatology colleagues across the globe should indulge in exploration, generation and documentation of evidence by conducting ethical research studies with large cohort size for the drugs that are being used off-label, that too based on limited evidence.

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