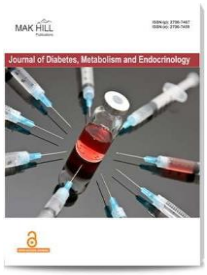

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Research Article

Fixed-Dose Combination (FDC) Formulations in the Indian Market Measured Against the National List of Essential Medicines 2022: A Document-Based Cross-Sectional Analysis.

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Abstract: ***Background:*** Fixed-dose combinations (FDCs) dominate India's pharmaceutical market, yet the National List of Essential Medicines (NLEM) admits few. This mismatch has not been quantified against NLEM 2022 and recent regulatory action. ***Objective:*** To characterise NLEM 2022 FDCs and compare them with FDCs marketed in India until their prohibition in August 2024, using NLEM 2022 and the WHO Model List of Essential Medicines (EML) 2023 as reference standards. ***Methods:*** Document-based cross-sectional study. Dataset A: all NLEM 2022 entries with ≥2 active ingredients in a fixed ratio. Dataset B: all 156 FDCs prohibited under Section 26A, Drugs and Cosmetics Act, 1940 (S.O. 3285(E)–3440(E), 2 August 2024). FDCs were coded for concordance, therapeutic area, route, ingredient count and ten component classes. Groups were compared with Mann–Whitney U and Fisher's exact tests. ***Results:*** NLEM 2022 contained 19 FDCs (4.9% of 384 medicines; 95% CI 3.2–7.6); 14 (73.7%) were anti-infectives and 17 had a WHO EML 2023 counterpart. None of the 156 prohibited FDCs matched an NLEM 2022 or WHO EML combination (0%; 95% CI 0–2.4). Prohibited FDCs were concentrated in dermatological (19.9%), ophthalmic/otic/nasal (19.2%), analgesic–musculoskeletal (16.0%) and cough-cold (15.4%) products, and contained more ingredients (median 3 [IQR 2–5; maximum 15] vs. 2 [IQR 2–2]; $p < 0.001$). Among prohibited FDCs, 70.5% had ≥3 ingredients versus 21.1% of NLEM FDCs (OR 8.97, 95% CI 2.71–24.69). Overall, 32.1% contained a vitamin, herbal or nutraceutical component, 21.8% a decongestant and 16.0% an antibacterial, antifungal or antiprotozoal agent. ***Conclusion:*** FDCs removed from the Indian market in 2024 had no overlap with the essential-medicines standard and were more complex and symptom-oriented than NLEM FDCs. Using NLEM/WHO EML criteria for FDC licensing, adding programme-critical FDCs (anti-tuberculosis, antihypertensive, inhaled corticosteroid–bronchodilator) to NLEM, and pharmacy-level audits are priorities.

Keywords: Fixed-dose combination; Essential medicines; NLEM 2022; Rational drug use; Drug regulation; Section 26A; Antimicrobial resistance; India.

INTRODUCTION

A fixed-dose combination (FDC) contains two or more active pharmaceutical ingredients in a fixed ratio within a single dosage form. Well-designed FDCs, such as antiretroviral, antimalarial and anti-tuberculosis combinations, simplify regimens, improve adherence and can delay the emergence of antimicrobial resistance (AMR). Poorly justified FDCs expose patients to unnecessary ingredients, prevent dose titration of individual components, multiply the risk of adverse drug reactions and interactions, and add cost without therapeutic gain [1,2].

India is among the largest FDC markets in the world. Using national sales data for 2011–2012, McGettigan and colleagues found that 124 NSAID FDC formulations were marketed, of which only 34 (27%) had been approved by the central regulator; 81% of antidepressant/benzodiazepine FDCs were unapproved and accounted for 69% of that segment's sales [3]. Among 118 antibiotic FDC formulations sold in India, 75 (64%) had never been approved by the Central Drugs Standard Control Organisation (CDSCO), and only four were approved in the United States or United Kingdom [4]. More recent longitudinal data show that psychotropic FDC sales rose from 0.8 to 1.4 billion standard units between 2008 and 2020, with unapproved formulations still accounting for 60.3% of those sales [5]. These findings reflect a historical gap between central approval and state-level manufacturing licences documented by Parliament in 2012 [6].

The National List of Essential Medicines (NLEM) is India's reference standard for medicines that satisfy priority health-care needs. NLEM 2022, released in September 2022, lists 384 medicines across 27 therapeutic sections [7,8]. Its inclusion criteria generally exclude FDCs unless the combination offers a proven advantage in efficacy, safety, adherence or resistance prevention over single agents [7]. NLEM listing has direct economic consequences: formulations of NLEM medicines fall under ceiling-price control through the Drugs (Prices Control) Order, 2013 [9]. Because a combination of a scheduled medicine with another ingredient was, in effect, a distinct product outside price control, FDCs have been described as a route by which manufacturers escape price regulation [2,10].

The Government of India has used Section 26A of the Drugs and Cosmetics Act, 1940 to prohibit irrational FDCs in several rounds: 344 FDCs in March 2016 following the Kokate committee review; 328 FDCs (with six restricted) in September 2018 after re-examination by the Drugs Technical Advisory Board (DTAB) under a Supreme Court direction; 14 FDCs in June 2023; and 156 FDCs in August 2024 [10–14]. Each prohibited FDC was, by definition, a licensed product that had been manufactured and sold in India. The published prohibition notifications therefore constitute a verifiable, product-level record of the FDCs that circulated in the Indian market.

Previous analyses of NLEM 2022 have noted that it contains few FDCs and omits the anti-tuberculosis FDCs used by the National TB Elimination Programme [15,16], while market studies have focussed on individual therapeutic classes [3–5,17]. To our knowledge, no study has compared the FDCs of NLEM 2022 directly with a complete, recent set of marketed FDCs. We therefore aimed (i) to enumerate and characterise the FDCs listed in NLEM 2022 and their concordance with the WHO Model List of Essential Medicines (EML) 2023, and (ii) to measure the concordance, therapeutic distribution and formulation complexity of the 156 FDCs removed from the Indian market in August 2024 relative to these essential-medicines standards. We hypothesised that marketed FDCs outside the essential-medicines standard would contain more ingredients and would be concentrated in symptomatic, over-the-counter-type therapeutic areas.

MATERIALS AND METHODS

Study design and reporting

This was a document-based (desk) cross-sectional study using publicly available regulatory and policy documents. Reporting follows the STROBE statement for cross-sectional studies, adapted to a document-level unit of analysis [18]. The unit of analysis was a single FDC entry (a unique combination of active ingredients as named in the source document).

Data sources

Reference standard. The National List of Essential Medicines 2022 (Ministry of Health and Family Welfare, Government of India), accessed as the CDSCO-hosted PDF [7], and the WHO Model List of Essential Medicines, 23rd list (2023) [19].

Market-side record. The CDSCO consolidated list of 156 FDCs prohibited for manufacture, sale and distribution under Section 26A of the Drugs and Cosmetics Act, 1940, by Gazette notifications S.O. 3285(E) to S.O. 3440(E) dated 2 August 2024 [14]. This is the most recent complete prohibition round and was used because every entry is a product that held a manufacturing licence and was marketed in India until the notification date; the list is publicly verifiable and item-numbered.

Contextual evidence. Published peer-reviewed analyses of Indian FDC sales and regulatory status (2015–2024) [3–5,17] and official or contemporaneous reports of earlier prohibition rounds [11–13] were extracted for descriptive comparison. All documents were accessed on 23 September 2026.

Eligibility and definitions

An NLEM entry was classified as an FDC if it named two or more active pharmaceutical ingredients combined in a fixed ratio in one product or co-packaged pack (e.g., "Amoxicillin + Clavulanic acid"). Parenteral fluids and electrolyte solutions (e.g., Ringer lactate), oral rehydration salts, and single drugs presented in a diluent (e.g., bupivacaine 0.5% with 7.5% glucose) were excluded because their components are not separate pharmacological agents in the sense relevant to FDC rationality. All 156 prohibited FDCs were included; none were excluded.

Concordance was defined as the identical combination of active ingredients appearing in NLEM 2022 or the WHO EML 2023, irrespective of strength. For NLEM entries, WHO EML status was coded as "listed", "equivalent listed" (a therapeutically interchangeable combination or the same components listed for co-administration, e.g., emtricitabine + tenofovir for lamivudine + tenofovir) or "not listed".

Variables and coding

For each prohibited FDC the following were coded: (a) primary therapeutic area (nine categories, assigned by pharmacological class of the principal active ingredient and the grouping used in the notification); (b) route (oral, topical skin, ophthalmic/otic/nasal, parenteral); (c) number of listed ingredients, counted as the ingredients named in the notification, including excipient-type substances listed as components (e.g., hydroxypropyl methylcellulose); and (d) presence of ten pre-specified component classes: antibacterial/antifungal/antiprotozoal agent; vitamin, mineral, herbal or nutraceutical; sympathomimetic decongestant; naphazoline; first-generation antihistamine; paracetamol; non-salicylate NSAID; proteolytic enzyme; galenical tincture, spirit or chloroform; and probiotic. A broader "any anti-infective" variable additionally counted antiparasitic agents (diethylcarbamazine, gamma benzene hexachloride). Component classes were identified by pre-specified keyword rules applied to the ingredient string and then checked manually item by item. For NLEM FDCs, the number of active ingredients and the number of listed formulation–strength combinations were recorded.

Bias and data quality

Selection bias was minimised by including every entry of both source documents. The complete coded dataset, the extraction rules and the analysis script are provided as supplementary material, so that every figure in this paper can be reproduced. Ingredient strings were transcribed from the official list; spelling errors in the source were corrected only where unambiguous (e.g., "Acelofenac"). Because the prohibited list is a record of FDCs judged irrational, it is not a random sample of all marketed FDCs; this is addressed in the limitations.

Statistical analysis

Categorical variables are presented as n (%) with Wilson score 95% CIs; the number of ingredients is presented as median (interquartile range, IQR) because it was right-skewed. The number of ingredients per FDC was compared between NLEM FDCs and prohibited FDCs with the two-sided Mann–Whitney U test (effect size: rank-biserial correlation, rrb). The proportions with ≥3 ingredients and with an anti-infective component were compared with Fisher's exact test, with odds ratios (OR) and Woolf 95% CIs (Haldane correction). Differences in ingredient count across therapeutic areas within the prohibited set were tested with the Kruskal–Wallis H test. A two-sided $p < 0.05$ was considered significant. Analyses were performed in Python 3 (pandas, SciPy 1.x, statsmodels) and figures in matplotlib.

Ethical considerations

The study used only publicly available government documents and published aggregate data; it involved no human participants, patient records or animals. Ethics committee approval was therefore not required.

RESULTS

FDCs in NLEM 2022

Of the 384 medicines in NLEM 2022, 19 entries met the FDC definition (4.9%; 95% CI 3.2–7.6) (Figure 1; Table 1). Anti-infectives accounted for 14 of 19 (73.7%; 95% CI 51.2–88.2): nine antiretroviral, three antibacterial (amoxicillin + clavulanic acid, piperacillin + tazobactam, co-trimoxazole) and two antimalarial combinations (Figure 2). The remaining five were lignocaine + adrenaline, ferrous salt + folic acid, ethinylestradiol + levonorgestrel, levodopa + carbidopa and coal tar + salicylic acid. Fifteen (78.9%) were two-drug combinations and four (21.1%) three-drug combinations. The 19 FDCs were listed in 46 formulation–strength combinations (median 2 per FDC; IQR 1–3).

Fourteen NLEM FDCs (73.7%) were listed in the WHO EML 2023 and three (15.8%) had an equivalent listed; only zidovudine + lamivudine + nevirapine and coal tar + salicylic acid had no WHO EML counterpart (Table 1). Conversely, several FDCs of the WHO EML 2023 were absent from NLEM 2022, including the first-line anti-tuberculosis FDCs, antihypertensive FDCs, cardiovascular "polypills", budesonide + formoterol, and the Reserve-group β-lactam/β-lactamase-inhibitor combinations (Table 2).

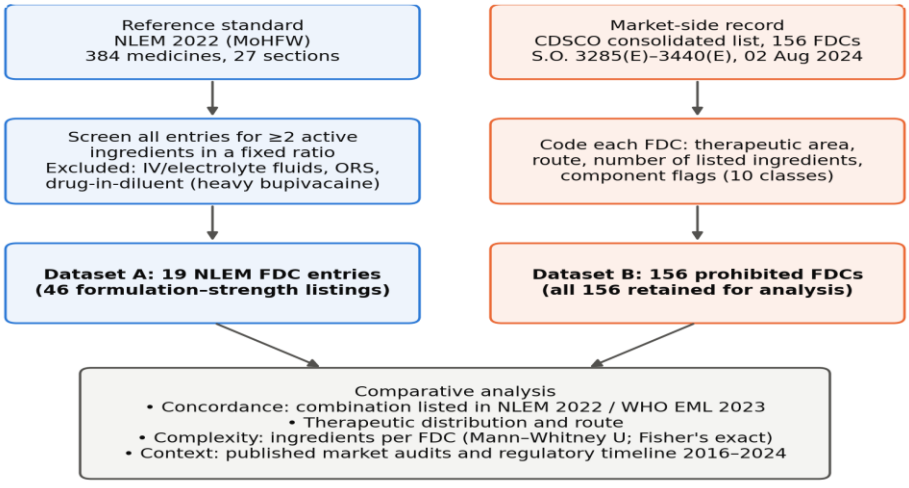

Figure 1. Study flow: data sources, eligibility rules and analytic steps. NLEM, National List of Essential Medicines; CDSCO, Central Drugs Standard Control Organisation; S.O., Statutory Order; WHO EML, World Health Organization Model List of Essential Medicines.

Table 1. Fixed-dose combination entries in the National List of Essential Medicines 2022 and their status in the WHO Model List of Essential Medicines 2023

NLEM 2022 code	FDC	Group	Active ingredients (n)	Formulation–strengths listed (n)	WHO EML 2023
6.2.1.2	Amoxicillin + Clavulanic acid	Antibacterial	2	5	Listed
6.2.1.13	Piperacillin + Tazobactam	Antibacterial	2	3	Listed
6.2.2.6	Sulphamethoxazole + Trimethoprim	Antibacterial	2	3	Listed
6.7.1.9	Zidovudine + Lamivudine	Antiretroviral	2	2	Listed
6.7.1.10	Zidovudine + Lamivudine + Nevirapine	Antiretroviral	3	2	Not listed
6.7.1.2	Abacavir + Lamivudine	Antiretroviral	2	2	Listed
6.7.1.5	Tenofovir DF + Lamivudine	Antiretroviral	2	1	Equivalent listed
6.7.1.6	Tenofovir DF + Lamivudine + Dolutegravir	Antiretroviral	3	1	Listed
6.7.1.7	Tenofovir DF + Lamivudine + Efavirenz	Antiretroviral	3	1	Listed
6.7.4.1	Atazanavir + Ritonavir	Antiretroviral	2	1	Listed
6.7.4.3	Darunavir + Ritonavir	Antiretroviral	2	1	Equivalent listed
6.7.4.4	Lopinavir + Ritonavir	Antiretroviral	2	4	Listed
6.10.1.1	Artemether + Lumefantrine	Antimalarial	2	3	Listed
6.10.1.3	Artesunate + Sulphadoxine-Pyrimethamine	Antimalarial	3	5	Equivalent listed
1.2.3	Lignocaine + Adrenaline	Local anaesthetic	2	2	Listed
8.1.3	Ferrous salt + Folic acid	Haematinic	2	3	Listed
18.2.1.1	Ethinylestradiol + Levonorgestrel	Contraceptive	2	1	Listed
5.3.1	Levodopa + Carbidopa	Antiparkinsonian	2	5	Listed
11.4.2	Coal tar + Salicylic acid	Dermatological	2	1	Not listed

"Equivalent listed": tenofovir + lamivudine (WHO lists emtricitabine + tenofovir, interchangeable NRTI backbone); darunavir + ritonavir (darunavir listed for co-administration with ritonavir); artesunate + sulphadoxine–pyrimethamine (sulfadoxine + pyrimethamine listed for use with artesunate). DF, disoproxil fumarate. Source: NLEM 2022 [7]; WHO EML 2023 [19].

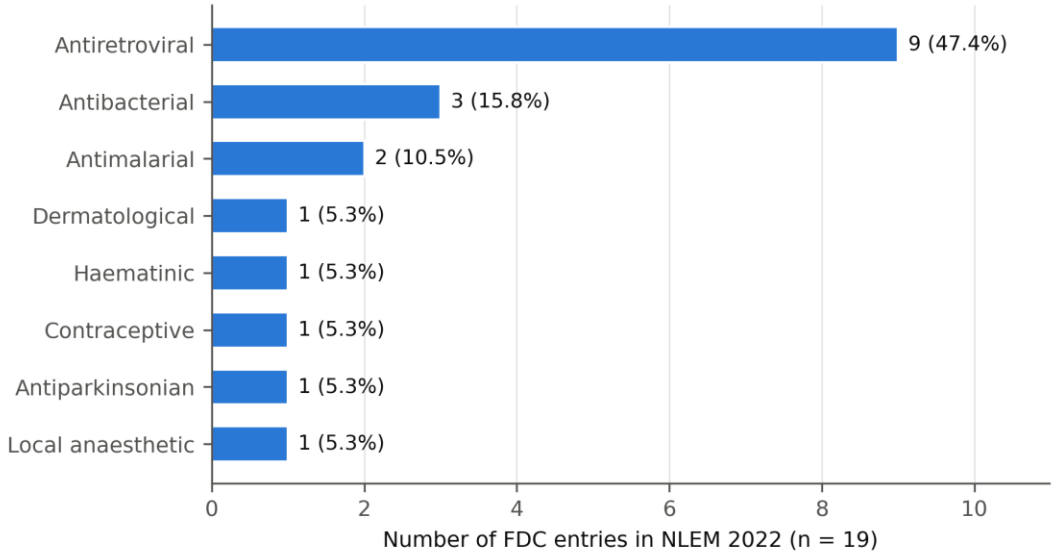

Figure 2. Distribution of the 19 fixed-dose combination entries in NLEM 2022 by therapeutic group. Anti-infectives (antiretroviral, antibacterial, antimalarial) account for 14/19 (73.7%).

Table 2. Selected FDCs in the WHO Model List of Essential Medicines 2023 that are absent from NLEM 2022

FDC in WHO EML 2023	Therapeutic use	Status in NLEM 2022
Ethambutol + isoniazid + pyrazinamide + rifampicin	Drug-susceptible TB, intensive phase (NTEP regimen)	Components listed singly; FDC absent
Isoniazid + pyrazinamide + rifampicin; isoniazid + rifampicin	Paediatric and continuation-phase TB	Components listed singly; FDC absent
Amlodipine + telmisartan (and other antihypertensive FDCs)	Hypertension	Absent
Cardiovascular polypills (statin + antihypertensive(s) ± aspirin)	Primary/secondary CVD prevention (added 2023)	Absent
Budesonide + formoterol	Asthma, COPD	Absent
Emtricitabine + tenofovir	HIV pre-exposure prophylaxis and treatment	Lamivudine-based equivalents listed
Artesunate + amodiaquine	Uncomplicated falciparum malaria	Absent
Ceftazidime + avibactam; meropenem + vaborbactam	Carbapenem-resistant Gram-negative infection (Reserve)	Absent

Source: WHO EML 2023 [19]; NLEM 2022 [7]; Manikandan 2023 [15]; PHRI 2023 [20]. NTEP, National Tuberculosis Elimination Programme; CVD, cardiovascular disease; COPD, chronic obstructive pulmonary disease.

Characteristics of marketed FDCs prohibited in 2024

The 156 prohibited FDCs were distributed across nine therapeutic areas (Figure 3; Table 3). The largest groups were dermatological topical products (31; 19.9%), ophthalmic, otic and nasal preparations (30; 19.2%), analgesic and musculoskeletal products (25; 16.0%) and cough-cold, respiratory and antiallergic products (24; 15.4%). Most were oral (92; 59.0%), followed by topical skin (31; 19.9%), ophthalmic/otic/nasal (30; 19.2%) and parenteral (3; 1.9%: mefenamic acid + paracetamol, diclofenac + thiocolchicoside and methocarbamol + diclofenac injections).

The median number of listed ingredients was 3 (IQR 2–5; mean 3.82 ± 2.02; range 2–15). Fifty FDCs (32.1%; 95% CI 25.2–39.7) had five or more ingredients; the most complex were a 15-enzyme digestive combination, a 12-ingredient glucosamine–chondroitin–vitamin–trace-element product and a 10-ingredient glucosamine product. Ingredient count differed across therapeutic areas (Kruskal–Wallis $H = 28.6$, $df = 8$, $p < 0.001$), being highest in ophthalmic/otic/nasal products (median 5; IQR 4–5) and gastrointestinal/hepatobiliary products (median 4.5; IQR 2.75–6.25) (Table 3).

Component analysis (Figure 5) showed that 50 FDCs (32.1%; 95% CI 25.2–39.7) contained a vitamin, mineral, herbal or nutraceutical ingredient (e.g., silymarin, Ginkgo biloba, glucosamine, aloe). Thirty-four (21.8%) contained a sympathomimetic decongestant, including 22 (14.1%) naphazoline-containing eye or nasal drops, and 29 (18.6%) a first-generation antihistamine. Paracetamol was present in 16 (10.3%) and a non-salicylate NSAID in 13 (8.3%); five combined paracetamol

with an NSAID. Seven (4.5%) contained a proteolytic enzyme (serratiopeptidase, bromelain or papain), three (1.9%) a probiotic, and three (1.9%) galenical tinctures or chloroform.

An antibacterial, antifungal or antiprotozoal agent was present in 25 FDCs (16.0%; 95% CI 11.1–22.6); 28 (17.9%) contained any anti-infective. These included systemic antibiotics combined with non-antibiotic adjuncts (cefixime + acetylcysteine; cephalexin + serratiopeptidase; doxycycline + serratiopeptidase; amoxicillin + dicloxacillin + Lactobacillus; erythromycin + lactic acid bacillus; doxycycline + ornidazole + bromelain + two probiotics), an antibiotic–antibiotic combination (tetracycline + colistin), an antibiotic–urinary antispasmodic combination (flavoxate + ofloxacin), topical antibiotic–corticosteroid–antifungal mixtures (miconazole + gentamicin + fluocinolone; beclomethasone + neomycin + clotrimazole + lignocaine) and a veterinary coccidiostat combination (sulfaquinoxaline + diaveridine + vitamin K).

Table 3. Characteristics of the 156 FDCs prohibited in August 2024, by therapeutic area

Therapeutic area	n (%)	Predominant route (n)	Ingredients, median (IQR)	Max	Any anti-infective, n
Dermatological (topical)	31 (19.9)	Topical (skin) (31)	3 (2.5–4.5)	9	14
Ophthalmic, otic & nasal	30 (19.2)	Ophthalmic/otic/nasal (30)	5 (4–5)	8	4
Analgesic & musculoskeletal	25 (16.0)	Oral (22)	3 (2–4)	12	0
Respiratory, cough-cold & antiallergic	24 (15.4)	Oral (24)	3 (2.75–4.25)	6	2
Gastrointestinal & hepatobiliary	16 (10.3)	Oral (16)	4.5 (2.75–6.25)	15	0
Neurological	10 (6.4)	Oral (10)	2 (2–3)	4	0
Reproductive & urological	8 (5.1)	Oral (8)	2 (2–3)	8	1
Systemic anti-infective	7 (4.5)	Oral (7)	3 (2–3)	5	7
Nutritional, metabolic & other	5 (3.2)	Oral (5)	2 (2–5)	5	0
Total	156 (100)	Oral (92)	3 (2–5)	15	28

IQR, interquartile range. Ingredients counted as named in the notification. Any anti-infective includes antibacterial, antifungal, antiprotozoal and antiparasitic agents. Kruskal–Wallis test for ingredient count across areas: H = 28.6, df = 8, p < 0.001.

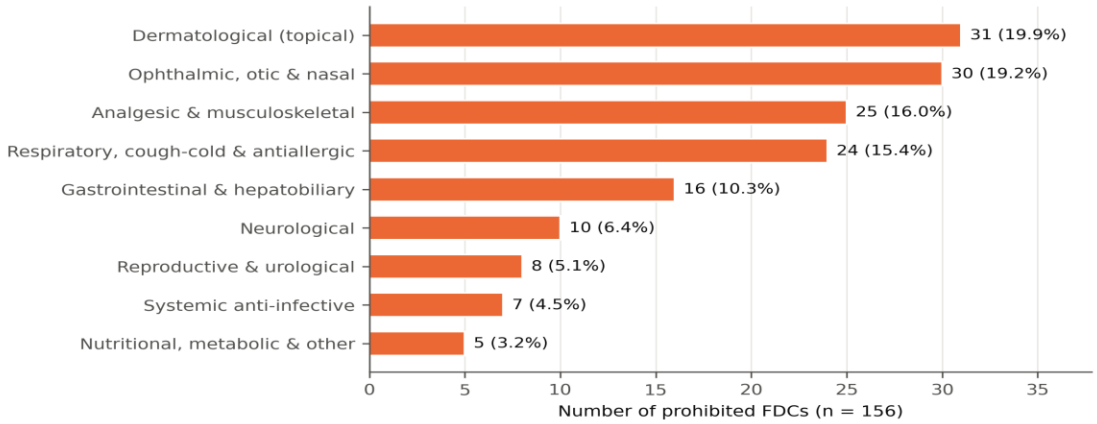

Figure 3. Therapeutic areas of the 156 FDCs prohibited under Section 26A of the Drugs and Cosmetics Act, 1940 (S.O. 3285(E)–3440(E), 2 August 2024) [14].

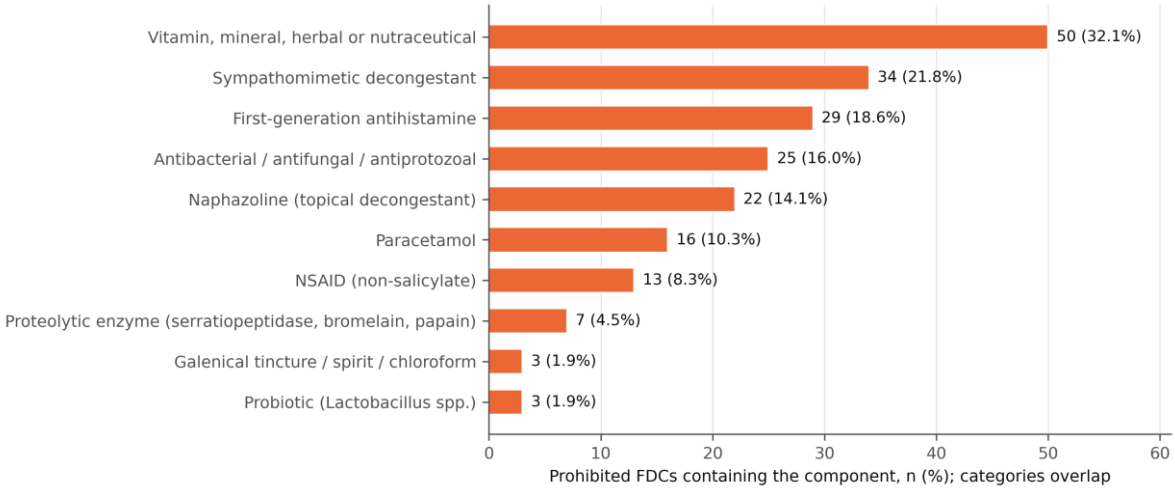

Figure 5. Pre-specified component classes present in the 156 prohibited FDCs. Categories are not mutually exclusive; naphazoline is a subset of sympathomimetic decongestants.

3.3 Concordance and comparative analysis

None of the 156 prohibited FDCs matched a combination in NLEM 2022 or the WHO EML 2023 (0/156; 95% CI 0–2.4%). Compared with the 19 NLEM FDCs, prohibited FDCs contained more ingredients (median 3 [IQR 2–5] vs. 2 [IQR 2–2]; Mann–Whitney U = 611, $p < 0.001$; $r_{rb} = 0.59$) (Figure 4). The odds of an FDC having ≥3 ingredients were 9.0 times higher among prohibited FDCs (110/156, 70.5% vs. 4/19, 21.1%; OR 8.97, 95% CI 2.71–24.69; $p < 0.001$). Conversely, anti-infectives made up most NLEM FDCs but a minority of prohibited FDCs (14/19, 73.7% vs. 28/156, 17.9%; OR 12.8, 95% CI 4.1–34.4; $p < 0.001$) (Table 4).

Table 4. Comparison of NLEM 2022 FDCs with FDCs prohibited in August 2024

Characteristic	NLEM 2022 FDCs (n = 19)	Prohibited FDCs, 2024 (n = 156)	Effect estimate (95% CI)	p-value
Combination listed in NLEM 2022 / WHO EML 2023, n (%)	19 (100) / 17 (89.5)*	0 (0) / 0 (0)	95% CI for 0/156: 0–2.4%	—
Ingredients per FDC, median (IQR)	2 (2–2)	3 (2–5)	$r_{rb} = 0.59$	< 0.001†
≥3 ingredients, n (%)	4 (21.1)	110 (70.5)	OR 8.97 (2.71–24.69)	< 0.001‡
≥5 ingredients, n (%)	0 (0)	50 (32.1)	—	—
Contains any anti-infective, n (%)	14 (73.7)	28 (17.9)	OR 12.8 (4.1–34.4)§	< 0.001‡
Vitamin/herbal/nutraceutical component, n (%)	0 (0)	50 (32.1)	—	—

*17/19 listed or with a listed therapeutic equivalent in WHO EML 2023 (14 listed; 3 equivalent). †Mann–Whitney U test; r_{rb}, rank-biserial correlation. ‡Fisher's exact test; OR with Woolf 95% CI (Haldane correction). §Odds of an anti-infective component in NLEM FDCs relative to prohibited FDCs. CI, confidence interval; OR, odds ratio.

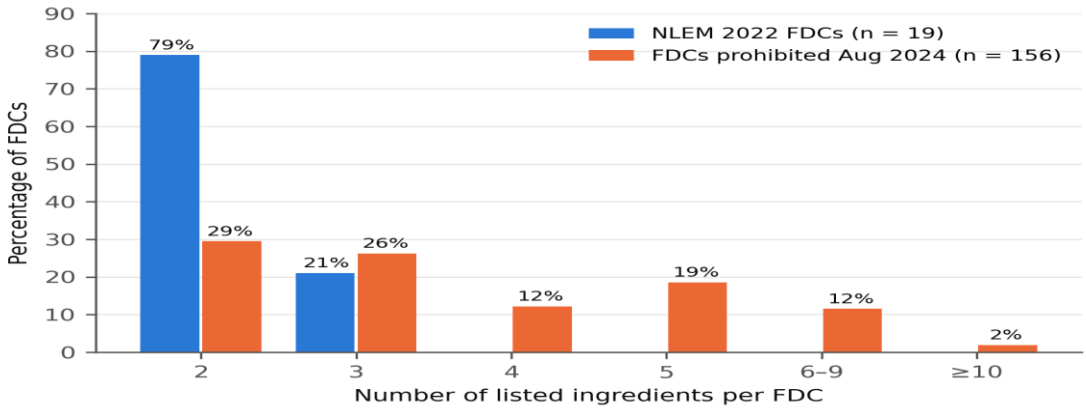

Figure 4. Number of listed ingredients per FDC: NLEM 2022 FDCs (n = 19) versus FDCs prohibited in August 2024 (n = 156). Bars show the percentage of FDCs in each group. Mann–Whitney U = 611, p < 0.001.

Regulatory and market context

Four rounds of Section 26A prohibitions were identified between 2016 and 2024 (Figure 6). These rounds are not additive: the 2018 notification re-examined the 2016 cohort after judicial review, and later rounds arose from expert-committee review of FDCs whose status remained unresolved. Published sales analyses (Table 5) show that unapproved FDCs made up 27–81% of formulations in the classes studied [3–5], that banned antimicrobial FDC sales fell by 75% within a year of the 2018 ban but that overall sales of discouraged FDCs fell by only 8% because of substitution with closely related combinations [17].

Table 5. Published evidence on FDCs in the Indian market, compared with the present study

Study (data period)	Market segment	Key quantitative finding
McGettigan et al., 2015 [3] (2011–12)	NSAID, metformin, psychotropic FDCs	NSAIDs: 124 formulations, 90 (73%) unapproved; antidepressant/benzodiazepine: 13/16 (81%) unapproved, 69% of segment sales
McGettigan et al., 2019 [4] (2007–12)	Antibiotic FDCs	118 formulations, 75 (64%) unapproved; 3,307 brands from 476 manufacturers; FDCs > one-third of antibiotic sales (872 million units, 2011–12)
Sulis et al., 2022 [17] (2018–19)	Antimicrobial FDCs banned in 2018	Sales of banned FDCs fell 75% (365 → 91 million units); all discouraged FDCs fell only 8% (2,467 → 2,265 million units)
Bogowicz et al., 2024 [5] (2008–20)	Psychotropic FDCs	Sales 0.8 → 1.4 billion units; unapproved share of sales 69.3% → 60.3%; 2 of 3 banned products still sold in 2020
Present study (notification 2024)	All therapeutic areas (156 prohibited FDCs)	0/156 concordant with NLEM 2022 or WHO EML 2023; median 3 ingredients (max 15); 32.1% contained nutraceutical components

Unapproved: no record of central (CDSCO) approval. Units are standard units (tablets, capsules, ampoules or equivalent) from national sales audits.

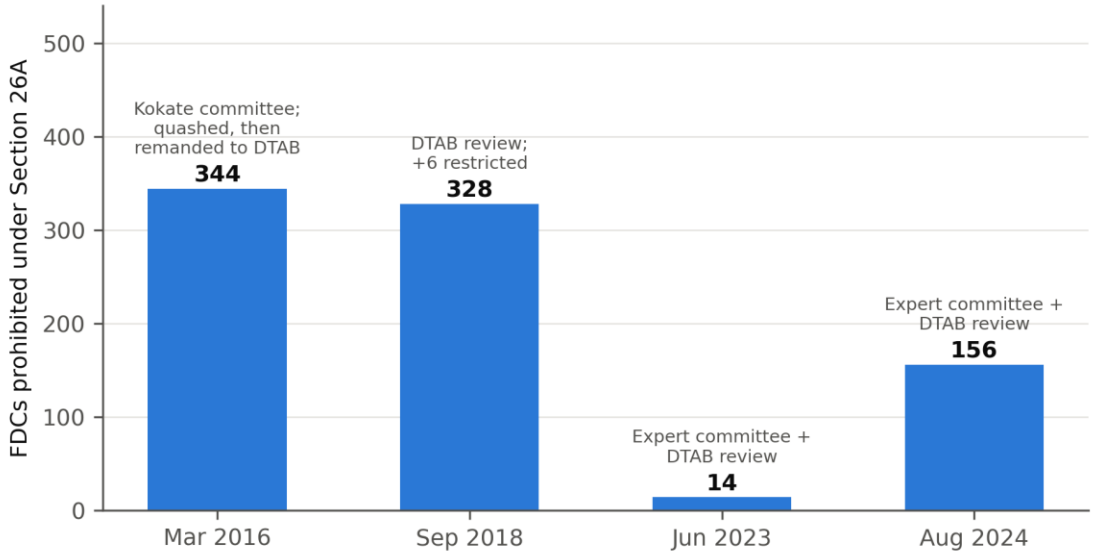

Figure 6. FDC prohibitions notified under Section 26A, 2016–2024 [10,12–14]. Rounds are not additive: the 2018 notification re-examined the 2016 cohort after judicial review. DTAB, Drugs Technical Advisory Board.

Supplementary Table S1. Complete coded list of the 156 FDCs prohibited by the Government of India on 2 August 2024 (S.O. 3285(E)–3440(E)); S. No. follows the CDSCO consolidated list [15]

S. No.	FDC (as notified)	Therapeutic area	Route	Ingredients (n)
1	Amylase + Protease + Glucoamylase + Pectinase + Alpha Galactosidase + Lactase + Beta-Gluconase + Cellulase + Lipase + Bromelain + Xylanase +	Gastrointestinal & hepatobiliary	Oral	15

	Hemicellulase + Malt diastase + Invertase + Papain			
2	Antimony Potassium Tartrate + Dried Ferrous Sulphate	Nutritional, metabolic & other	Oral	2
3	Benfotiamine + Silymarin + L-Ornithine L-aspartate + Sodium Selenite + Folic acid + Pyridoxine hydrochloride	Gastrointestinal & hepatobiliary	Oral	6
4	Bismuth Ammonium Citrate + Papain	Gastrointestinal & hepatobiliary	Oral	2
5	Cyproheptadine HCl + Thiamine HCl + Riboflavine + Pyridoxine HCl + Niacinamide	Nutritional, metabolic & other	Oral	5
6	Cyproheptadine Hydrochloride + Tricholine Citrate + Thiamine Hydrochloride + Riboflavine + Pyridoxine Hydrochloride	Nutritional, metabolic & other	Oral	5
7	Rabeprazole Sodium (As enteric coated tablet) + Clidinium Bromide + Dicyclomine HCl + Chlordiazepoxide	Gastrointestinal & hepatobiliary	Oral	4
8	Fungal Diastase + Papain + Nux vomica Tincture + Cardamom Tincture + Casein Hydrolysed + Alcohol	Gastrointestinal & hepatobiliary	Oral	6
9	Mefenamic Acid + Paracetamol Injection	Analgesic & musculoskeletal	Parenteral	2
10	Omeprazole Magnesium + Dicyclomine HCl	Gastrointestinal & hepatobiliary	Oral	2
11	S-adenosyl methionine + Metadoxine + Ursodeoxycholic acid BP + L-Methylfolate Calcium eq. to L-Methylfolate + Choline bitartrate + Silymarin + L-ornithine L-aspartate + Inositol + Taurine	Gastrointestinal & hepatobiliary	Oral	9
12	Silymarin + Thiamine Mononitrate + Riboflavin + Pyridoxine HCl + Niacinamide + Calcium pantothenate + Vitamin B12	Gastrointestinal & hepatobiliary	Oral	7
13	Silymarin + Pyridoxine HCl + Cyanocobalamin + Niacinamide + Folic Acid	Gastrointestinal & hepatobiliary	Oral	5
14	Silymarin + Vitamin B6 + Vitamin B12 + Niacinamide + Folic acid + Tricholine Citrate	Gastrointestinal & hepatobiliary	Oral	6
15	Sodium Citrate + Citric Acid Monohydrate Flavored with Cardamom Oil, Caraway Oil, Cinnamon Oil, Clove Oil, Ginger Oil + Alcohol	Reproductive & urological	Oral	8
16	Sucralfate + Aceclofenac	Gastrointestinal & hepatobiliary	Oral	2
17	Sucralfate + Domperidone + Dimethicone	Gastrointestinal & hepatobiliary	Oral	3
18	Sucralfate + Domperidone	Gastrointestinal & hepatobiliary	Oral	2

19	Tincture Ipecacuanha + Tincture Urgenia + Camphorated Opium Tincture + Aromatic Spirit of Ammonia + Chloroform + Alcohol	Respiratory, cough-cold & antiallergic	Oral	6
20	Ursodeoxycholic Acid + Metformin HCl	Nutritional, metabolic & other	Oral	2
21	Weak Ginger tincture + Aromatic Spirit of Ammonia + Peppermint Spirit + Chloroform + Sodium Bicarbonate + Compound Cardamom + Alcohol	Gastrointestinal & hepatobiliary	Oral	7
22	Sucralfate + Pantoprazole Sodium + Zinc Gluconate + Light Magnesium Carbonate	Gastrointestinal & hepatobiliary	Oral	4
23	Aloe + Vitamin E Soap	Dermatological (topical)	Topical (skin)	2
24	Povidone Iodine + Metronidazole + Aloe	Dermatological (topical)	Topical (skin)	3
25	Azelaic acid + Tea Tree Oil + Salicylic acid + Allantoin + Zinc oxide + Aloe vera + Jojoba oil + Vitamin E + Soap noodles	Dermatological (topical)	Topical (skin)	9
26	Azithromycin + Adapalene	Dermatological (topical)	Topical (skin)	2
27	Calamine + Aloes + Allantoin	Dermatological (topical)	Topical (skin)	3
28	Calamine + Diphenhydramine Hydrochloride + Aloe + Glycerine + Camphor	Dermatological (topical)	Topical (skin)	5
29	Chlorphenesin + Zinc oxide + Starch	Dermatological (topical)	Topical (skin)	3
30	Clindamycin Phosphate + Zinc acetate	Dermatological (topical)	Topical (skin)	2
31	Gamma Benzene Hexachloride + Benzocaine	Dermatological (topical)	Topical (skin)	2
32	Glucosamine hydrochloride + Diacerein + Menthol + Camphor + Capsaicin	Dermatological (topical)	Topical (skin)	5
33	Hydroquinone 2.0% w/w + Octyl Methoxycinnamate 5.0% w/w + Oxybenzone 30 % w/w	Dermatological (topical)	Topical (skin)	3
34	Ketoconazole + Zinc Pyrithione + D-Panthenol + Tea Tree Oil + Aloes	Dermatological (topical)	Topical (skin)	5
35	Ketoconazole + Aloe vera + Vitamin A Acetate	Dermatological (topical)	Topical (skin)	3
36	Ketoconazole + Aloes + ZPTO	Dermatological (topical)	Topical (skin)	3
37	Kojic Acid + Arbutin + Octinoxate + Vitamin E + Mulberry	Dermatological (topical)	Topical (skin)	5
38	Lornoxicam + Capsaicin + Menthol + Camphor	Dermatological (topical)	Topical (skin)	4
39	Lornoxicam + Thiocolchicoside + Oleum Lini + Menthol + Methyl salicylate	Dermatological (topical)	Topical (skin)	5

40	Menthol + Aloe vera Topical Spray	Dermatological (topical)	Topical (skin)	2
41	Menthol + Lignocaine HCl + Aloe vera gel + Clotrimazole + Diphenhydramine	Dermatological (topical)	Topical (skin)	5
42	Miconazole nitrate + Gentamicin + Fluocinolone Acetonide + Zinc Sulphate	Dermatological (topical)	Topical (skin)	4
43	Miconazole + Tinidazole	Dermatological (topical)	Topical (skin)	2
44	Minoxidil + Aminexil + Alcohol	Dermatological (topical)	Topical (skin)	3
45	Minoxidil + Azelaic acid + Saw palmetto	Dermatological (topical)	Topical (skin)	3
46	Minoxidil + Aminexil	Dermatological (topical)	Topical (skin)	2
47	Pine Bark extract + Kojic acid + Sodium Ascorbyl Phosphate	Dermatological (topical)	Topical (skin)	3
48	Povidone Iodine + Tinidazole + Zinc sulphate	Dermatological (topical)	Topical (skin)	3
49	Povidone Iodine + Ornidazole + Dexpanthenol	Dermatological (topical)	Topical (skin)	3
50	Salicylic acid + Aloe vera + Allantoin + D-Panthenol	Dermatological (topical)	Topical (skin)	4
51	Silver sulphadiazine + Chlorhexidine Gluconate solution + Allantoin + Aloe vera gel + Vitamin E acetate	Dermatological (topical)	Topical (skin)	5
52	Sodium salicylate + Zinc gluconate + Pyridoxine HCl	Dermatological (topical)	Topical (skin)	3
53	Tetracycline + Colistin Sulphate	Dermatological (topical)	Topical (skin)	2
54	Clomiphene + Ubidecarenone	Reproductive & urological	Oral	2
55	Combikit of Clomiphene Citrate + Estradiol Valerate	Reproductive & urological	Oral	2
56	Flavoxate HCl + Ofloxacin	Reproductive & urological	Oral	2
57	Clomiphene Citrate + N-Acetylcysteine	Reproductive & urological	Oral	2
58	Evening Primrose Oil + Cod liver oil	Reproductive & urological	Oral	2
59	Sildenafil Citrate + Papaverine + L-Arginine	Reproductive & urological	Oral	3
60	Tranexamic acid + Mefenamic acid + Vitamin K1	Reproductive & urological	Oral	3
61	Divalproex Sodium + Oxcarbazepine	Neurological	Oral	2
62	Divalproex Sodium + Levetiracetam	Neurological	Oral	2
63	Ergotamine tartrate + Caffeine + Paracetamol + Prochlorperazine maleate	Neurological	Oral	4
64	Piracetam + Ginkgo biloba extracts + Vinpocetine	Neurological	Oral	3
65	Ginkgo biloba + Methylcobalamin	Neurological	Oral	2

66	Ginkgo biloba + Methylcobalamin + Alpha lipoic acid + Pyridoxine HCl	Neurological	Oral	4
67	Ginseng Extract + Dried extract of Ginkgo Biloba	Neurological	Oral	2
68	Meclizine HCl + Paracetamol + Caffeine	Neurological	Oral	3
69	Nicergoline + Vinpocetine	Neurological	Oral	2
70	Gamma Linolenic Acid + Methylcobalamin	Neurological	Oral	2
71	Beclomethasone Dipropionate + Neomycin Sulphate + Clotrimazole + Lignocaine HCl	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	4
72	Boric acid + Phenylephrine HCl + Naphazoline Nitrate + Menthol + Camphor	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	5
73	Naphazoline HCl + Chlorpheniramine Maleate + Zinc Sulphate + Hydroxy Propyl Methyl Cellulose	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	4
74	Chlorpheniramine Maleate + Naphazoline HCl + Zinc Sulphate + Sodium Chloride + Hydroxy Propyl Methyl Cellulose	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	5
75	Chlorpheniramine Maleate + Naphazoline HCl + Hydroxy Propyl Methyl Cellulose	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	3
76	Chlorpheniramine Maleate + Sodium Chloride + Boric Acid + Tetrahydrozoline HCl	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	4
77	Chlorpheniramine Maleate + Phenylephrine HCl + Antipyrine	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	3
78	Ketorolac Tromethamine + Chlorpheniramine Maleate + Phenylephrine HCl + Hydroxy Propyl Methyl Cellulose	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	4
79	Ketorolac Tromethamine + Fluorometholone	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	2
80	Naphazoline HCl + Zinc Sulphate + Boric Acid + Sodium Chloride + Chlorpheniramine Maleate	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	5
81	Naphazoline HCl + Hydroxy Propyl Methyl Cellulose + Boric Acid + Borax + Menthol + Camphor	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	6
82	Naphazoline HCl + Hydroxy Propyl Methyl Cellulose + Chlorpheniramine Maleate + Boric Acid + Sodium Chloride + Zinc Sulphate	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	6
83	Naphazoline HCl + Hydroxy Propyl Methyl Cellulose + Chlorpheniramine Maleate + Boric Acid	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	4
84	Naphazoline HCl + Chlorpheniramine Maleate + Methyl Cellulose	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	3
85	Naphazoline HCl + Hydroxy	Ophthalmic, otic &	Ophthalmic/otic/nasal	5

	Methyl Cellulose + Boric Acid + Menthol + Camphor	nasal		
86	Naphazoline HCl + Boric Acid + Menthol + Camphor + Methyl Cellulose + Chlorpheniramine Maleate + Zinc Sulphate + Sodium Chloride	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	8
87	Naphazoline HCl + Phenylephrine HCl + HPMC + Chlorpheniramine Maleate + Menthol + Camphor	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	6
88	Naphazoline HCl + Hydroxy Propyl Methyl Cellulose + Chlorpheniramine Maleate + Boric Acid + Sodium Chloride + Zinc Sulphate + Menthol + Camphor	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	8
89	Naphazoline HCl + Hydroxy Propyl Methyl Cellulose + Chlorpheniramine Maleate + Boric Acid + Zinc Sulphate	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	5
90	Naphazoline HCl + Azelastine HCl + Sodium Carboxy Methyl Cellulose + Menthol + Camphor + Stabilized Oxychloro complex	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	6
91	Naphazoline HCl + Sodium Carboxy Methyl Cellulose + Menthol + Camphor + Stabilized Oxychloro complex	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	5
92	Naphazoline Nitrate + Chlorpheniramine Maleate + Phenylephrine HCl + Hydroxy Methyl Cellulose + Boric Acid + Menthol + Camphor	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	7
93	Naphazoline Nitrate + Chlorpheniramine Maleate + Zinc Sulphate + Boric Acid + Sodium Chloride	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	5
94	Norfloxacin + Tinidazole (with Betacyclodextrin) Eye ointment	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	2
95	Ofloxacin + Beclomethasone Dipropionate + Lignocaine HCl	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	3
96	Naphazoline HCl + Chlorpheniramine Maleate + Phenylephrine HCl + Menthol + Camphor	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	5
97	Phenylephrine HCl + Naphazoline HCl + Menthol + Camphor + Hydroxy Propyl Methyl Cellulose	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	5
98	Phenylephrine HCl + Naphazoline HCl + Menthol + Camphor	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	4
99	Sulphacetamide Sodium + Zinc Sulphate + Chlorpheniramine Maleate + Boric acid + Sodium Chloride	Ophthalmic, otic & nasal	Ophthalmic/otic/nasal	5
100	Zinc Sulphate + Boric acid +	Ophthalmic, otic &	Ophthalmic/otic/nasal	5

	Naphazoline HCl + Sodium Chloride + Phenyl Ethyl Alcohol	nasal		
101	Cetirizine HCl + Paracetamol + Phenylephrine HCl	Respiratory, cough-cold & antiallergic	Oral	3
102	Cetirizine HCl + Phenylephrine HCl	Respiratory, cough-cold & antiallergic	Oral	2
103	Levocetirizine + Phenylephrine HCl	Respiratory, cough-cold & antiallergic	Oral	2
104	Levocetirizine + Phenylephrine HCl + Paracetamol	Respiratory, cough-cold & antiallergic	Oral	3
105	Phenylephrine HCl + Paracetamol + Levocetirizine HCl + Menthol	Respiratory, cough-cold & antiallergic	Oral	4
106	Levocetirizine HCl + Ambroxol HCl + Paracetamol	Respiratory, cough-cold & antiallergic	Oral	3
107	Levocetirizine HCl + Ambroxol HCl + Phenylephrine HCl	Respiratory, cough-cold & antiallergic	Oral	3
108	Diethylcarbamazine Citrate + Chlorpheniramine maleate	Respiratory, cough-cold & antiallergic	Oral	2
109	Diethylcarbamazine Citrate + Levocetirizine HCl	Respiratory, cough-cold & antiallergic	Oral	2
110	Ambroxol HCl + Phenylephrine HCl + Guaiphenesin	Respiratory, cough-cold & antiallergic	Oral	3
111	Bromhexine HCl + Phenylephrine HCl	Respiratory, cough-cold & antiallergic	Oral	2
112	Etofylline + Theophylline anhydrous eq. to Theophylline hydrate + Ambroxol HCl	Respiratory, cough-cold & antiallergic	Oral	3
113	Etofylline + Theophylline anhydrous eq. to Theophylline hydrate + Montelukast	Respiratory, cough-cold & antiallergic	Oral	3
114	Ambroxol HCl + Terbutaline Sulphate + Ammonium Chloride + Guaiphenesin + Menthol	Respiratory, cough-cold & antiallergic	Oral	5
115	Ambroxol HCl + Salbutamol Sulphate + Ammonium Chloride + Guaiphenesin + Menthol	Respiratory, cough-cold & antiallergic	Oral	5
116	Cetirizine HCl + Terbutaline Sulphate + Ambroxol HCl + Guaiphenesin	Respiratory, cough-cold & antiallergic	Oral	4
117	Dextromethorphan Hydrobromide + Chlorpheniramine Maleate + Ammonium Chloride + Sodium Citrate + Menthol	Respiratory, cough-cold & antiallergic	Oral	5
118	Salbutamol Sulphate + Bromhexine HCl + Guaiphenesin + Ammonium Chloride + Menthol	Respiratory, cough-cold & antiallergic	Oral	5
119	Terbutaline Sulphate + Bromhexine HCl + Chlorpheniramine Maleate	Respiratory, cough-cold & antiallergic	Oral	3
120	Chlorpheniramine Maleate + P.G. Sulphonate + Ammonium Chloride + Sodium Citrate + Menthol	Respiratory, cough-cold & antiallergic	Oral	5
121	Aminophylline + Ammonium Chloride + Sodium Citrate	Respiratory, cough-cold & antiallergic	Oral	3

122	Paracetamol + Chlorpheniramine Maleate + Phenyl Propanolamine	Respiratory, cough-cold & antiallergic	Oral	3
123	Trithioparamethoxyphenyl Propene + Chlorpheniramine Maleate	Respiratory, cough-cold & antiallergic	Oral	2
124	Aceclofenac 50 mg + Paracetamol 125 mg oral liquid	Analgesic & musculoskeletal	Oral	2
125	Aceclofenac 50 mg + Paracetamol 125 mg tablet	Analgesic & musculoskeletal	Oral	2
126	Adenosine triphosphate diphosphate + Magnesium Orotate	Nutritional, metabolic & other	Oral	2
127	Amoxicillin Trihydrate + Dicloxacillin Sodium + Lactobacillus	Systemic anti-infective	Oral	3
128	Camylofin Dihydrochloride 25 mg + Paracetamol 300 mg	Analgesic & musculoskeletal	Oral	2
129	Cefixime + Acetyl Cysteine	Systemic anti-infective	Oral	2
130	Cephalexin Monohydrate + Serratiopeptidase	Systemic anti-infective	Oral	2
131	Cetyl Myristoleate + Glucosamine Sulphate Potassium + Methyl Sulfonyl Methane	Analgesic & musculoskeletal	Oral	3
132	Diacerein IP + Glucosamine Sulphate Potassium Chloride USP + MSM (Methylsulphonyl Methane) + Cetyl Myristoleate	Analgesic & musculoskeletal	Oral	4
133	Paracetamol + Diclofenac Potassium + Caffeine Anhydrous	Analgesic & musculoskeletal	Oral	3
134	Diclofenac sodium + Thiocolchicoside Injection	Analgesic & musculoskeletal	Parenteral	2
135	Doxycycline + Ornidazole + Bromelain + Lactobacillus Rhamnosus + Lactobacillus Reuteri RC	Systemic anti-infective	Oral	5
136	Doxycycline HCl + Betacyclodextrin + Serratiopeptidase	Systemic anti-infective	Oral	3
137	Erythromycin stearate eq. to Erythromycin + Lactic acid Bacillus	Systemic anti-infective	Oral	2
138	Etodolac + Paracetamol + Serratiopeptidase	Analgesic & musculoskeletal	Oral	3
139	Flupirtine Maleate 400 mg + Paracetamol 325 mg tablet	Analgesic & musculoskeletal	Oral	2
140	Glucosamine sulphate potassium chloride 410 mg + Chondroitin Sulphate 100 mg	Analgesic & musculoskeletal	Oral	2
141	Glucosamine sulphate potassium chloride + Methyl Sulphonyl Methane (MSM) + Sodium Borate + Copper Sulphate pentahydrate + Manganese Sulphate + Vitamin	Analgesic & musculoskeletal	Oral	6

	D3			
142	Glucosamine Sulphate + Sodium chloride + Manganese + Boron + Zinc + Copper	Analgesic & musculoskeletal	Oral	6
143	Glucosamine sulphate + Chondroitin sulphate + Methylsulfonylmethane + Vitamin D3 + Vitamin E + Vitamin C + Selenium + Elemental Zinc + Elemental Manganese + Elemental Chromium + Elemental Copper + Elemental Boron	Analgesic & musculoskeletal	Oral	12
144	Glucosamine sulphate + Methyl sulfonyl methane + Manganese sulphate + Vit E acetate + Calcium Carbonate	Analgesic & musculoskeletal	Oral	5
145	Glucosamine Sulphate + Vitamin E acetate + Calcium Pantothenate + Vitamin D3	Analgesic & musculoskeletal	Oral	4
146	Glucosamine Sulphate Potassium chloride + Calcium Carbonate from an organic source (oyster shell) eq. to elemental calcium + Vitamin D3	Analgesic & musculoskeletal	Oral	3
147	Cetyl Myristoleate + Glucosamine Sulphate Potassium chloride + Methyl sulfonyl methane	Analgesic & musculoskeletal	Oral	3
148	Glucosamine Sulphate Potassium chloride + Methyl sulfonyl methane + Calcium carbonate + Vitamin E + Manganese	Analgesic & musculoskeletal	Oral	5
149	Glucosamine Sulphate Potassium chloride + Calcium carbonate + Methyl sulfonyl methane + Vit D3	Analgesic & musculoskeletal	Oral	4
150	Glucosamine Sulphate Potassium + Methyl sulphate Sodium + Sulphonyl Methane + Chondroitin Sulphate Sodium + Calcium Carbonate + Vitamin D3 + Sodium Borate + Cupric Oxide + Colloidal Silicon Dioxide + Manganese Chloride	Analgesic & musculoskeletal	Oral	10
151	Methocarbamol + Diclofenac Sodium Injection	Analgesic & musculoskeletal	Parenteral	2
152	Paracetamol + Pentazocine	Analgesic & musculoskeletal	Oral	2
153	Sucralfate + Domperidone + Simethicone	Gastrointestinal & hepatobiliary	Oral	3
154	Sulfaquinoxaline + Diaveridine HCl + Vitamin K	Systemic anti-infective	Oral	3
155	Tramadol HCl + Dicyclomine HCl + Domperidone	Analgesic & musculoskeletal	Oral	3
156	Tramadol HCl + Paracetamol + Caffeine + Taurine	Analgesic & musculoskeletal	Oral	4

Area and route assigned by the author as described in Methods. Ingredient names reproduced from the CDSCO list; minor spelling corrections only. Full coded variables (ten component flags) are provided in datasetB_prohibited_2024.csv.

DISCUSSION

This analysis produced three principal findings. First, NLEM 2022 contains only 19 FDCs (4.9% of listed medicines), and these are almost all programme-critical anti-infective combinations with a WHO EML counterpart. Second, the 156 FDCs removed from the Indian market in August 2024 had no overlap with either essential-medicines list. Third, the marketed FDCs were structurally different from the essential ones: they had nine-fold higher odds of containing three or more ingredients, one in three contained a vitamin, herbal or nutraceutical component, and they were concentrated in symptomatic therapeutic areas—topical skin products, decongestant eye drops, analgesic–musculoskeletal and cough-cold products—where self-medication and over-the-counter sale are common.

The contrast in composition reflects the different logics by which the two sets of FDCs came into existence. NLEM FDCs satisfy WHO criteria: each component has demonstrated efficacy, the combination has a proven advantage (for example, preventing monotherapy and resistance in HIV and malaria, or peripheral decarboxylase inhibition in levodopa + carbidopa), and the ratio is fixed at clinically appropriate doses [2,19]. By contrast, the prohibited FDCs typically added symptomatic, adjunctive or non-evidence-based ingredients to an established drug—for example, serratiopeptidase, for which a systematic review found no reliable evidence of anti-inflammatory benefit [21], added to cephalexin, doxycycline or etodolac. Naphazoline, an imidazoline vasoconstrictor associated with rebound hyperaemia and, in young children, systemic toxicity, appeared in 22 ophthalmic and nasal products combined with antihistamines, camphor, menthol and boric acid. Such combinations cannot be titrated, expose patients to ingredients they do not need and complicate attribution of adverse reactions [1,10].

The presence of antimicrobials in 16% of prohibited FDCs is directly relevant to AMR containment. Antibiotic FDCs of unproven rationale are classified by WHO as "not recommended" in the AWaRe framework [22], and India has repeatedly been identified as a major consumer of such products [4,17]. Our data show that the 2024 prohibition removed a further set of systemic antibiotic–adjunct and topical antibiotic–corticosteroid combinations, and that one prohibited product was a veterinary coccidiostat combination. The experience after the 2018 ban is instructive: sales of the banned antimicrobial FDCs fell by 75%, but manufacturers substituted closely related, non-banned combinations, so that total sales of discouraged FDCs fell by only 8% [17]. Product-by-product prohibition therefore addresses the symptom rather than the licensing pathway that allows new variants to appear.

Our findings also point to gaps on the NLEM side. NLEM 2022 lists first-line anti-tuberculosis drugs only as single agents, although the National TB Elimination Programme uses 3- and 4-drug FDCs and the WHO EML lists them [15,19]. Antihypertensive FDCs, cardiovascular polypills (added to the WHO EML in 2023) and budesonide + formoterol inhalers are similarly absent [19,20]. These are precisely the FDCs for which there is evidence of improved adherence and outcomes. Their omission means that the most rational FDCs used in Indian practice fall outside the price-control and public-procurement benefits that NLEM listing confers [9], while irrational FDCs historically escaped price control by virtue of not being listed [2,10]. Revising NLEM to include programme-critical FDCs would align the essential-medicines standard with national programmes and with the WHO EML.

Our results are consistent with earlier Indian studies. McGettigan and colleagues showed that most NSAID, psychotropic and antibiotic FDC formulations on the market had never been centrally approved [3,4], and Bogowicz and colleagues found that unapproved formulations still accounted for 60% of psychotropic FDC sales in 2020 and that two of three banned psychotropic FDCs remained on sale [5]. Rao and Hotwani, counting FDC entries in NLEM 2022 with broader inclusion rules, reported 22 FDCs, nine of them antiretroviral [16]; the difference from our 19 is explained by our exclusion of oral rehydration salts, parenteral solutions and drug-in-diluent preparations. Our study extends this literature by providing a complete, item-level comparison of a recent regulatory cohort with the essential-medicines standard.

Clinical and policy implications. For prescribers and pharmacists, the absence of any prohibited FDC from the NLEM/WHO EML provides a simple screening heuristic: an FDC that is not on the essential-medicines list should be prescribed only when each ingredient is independently indicated at the fixed dose. For regulators, the findings support (i) mandatory demonstration of therapeutic justification under the New Drugs and Clinical Trials Rules, 2019 for all FDCs, including those licensed by states before 2019 [23]; (ii) a public, searchable register of licensed FDCs linked to the NLEM; and (iii) post-ban market surveillance to detect substitution. For institutional drug and therapeutics committees and AMR stewardship programmes, hospital formularies should restrict antibiotic FDCs to those in the NLEM/WHO EML.

Strengths and limitations. Strengths include the use of complete, official, publicly verifiable documents; inclusion of every entry without sampling; pre-specified definitions; and full reproducibility of the dataset and code. Several limitations apply.

First, the market-side dataset consists of FDCs already judged irrational by an expert committee; it is a verifiable record of marketed FDCs but not a representative sample of all FDCs currently sold, and it cannot provide sales volumes, brand counts or local availability. Findings should not be extrapolated to the proportion of all marketed FDCs that are irrational. Second, we did not conduct a pharmacy-level survey in a defined geographic area, so regional variation in FDC availability could not be assessed. Third, ingredient counts followed the notification text, which lists some excipient-type substances as ingredients; this may slightly overstate complexity for ophthalmic products. Fourth, therapeutic-area coding involved investigator judgement for some multi-purpose products, although the coding rules and the full coded list are provided. Finally, concordance with the WHO EML was assessed at the level of the active-ingredient combination and did not consider strength or formulation.

Future research. Prospective, geographically defined audits of retail pharmacy stock and prescriptions, using NLEM 2022 as the reference standard, are needed to estimate the share of irrational FDCs currently dispensed, to track substitution after prohibitions, and to quantify the proportion of antibiotic FDCs in community use. Linking such audits to AMR surveillance under the national AMR containment programme would allow the effect of FDC regulation on resistance trends to be assessed.

CONCLUSION

NLEM 2022 includes only 19 FDCs, almost all anti-infective combinations of proven value and concordant with the WHO EML. The 156 FDCs removed from the Indian market in 2024 shared no combination with either essential-medicines list and were significantly more complex, symptomatic and nutraceutical in composition. Using the NLEM and WHO EML as the licensing benchmark for FDCs, adding programme-critical FDCs (anti-tuberculosis, antihypertensive, inhaled corticosteroid–bronchodilator) to the NLEM, and monitoring the market for substitution after prohibitions are practical steps to promote rational use and support AMR containment.

Declarations

Ethics approval: Not applicable. The study used publicly available documents and published aggregate data only and involved no human participants or animals.
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Conflicts of interest: The author declares no conflicts of interest.
Author contribution: AN conceived and designed the study, extracted and coded the data, performed the statistical analysis, and wrote and approved the final manuscript.
Data availability: The complete coded datasets (NLEM 2022 FDC entries; 156 prohibited FDCs with all coded variables) and the analysis script are provided as supplementary files (Supplementary Table S1; datasetA_nlem2022_fdcs.csv; datasetB_prohibited_2024.csv; analysis.py).
Use of AI tools: An AI assistant (Claude, Anthropic) was used to support data extraction from public documents, coding, statistical programming and language editing. The author verified all data, analyses and references and takes full responsibility for the content.

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