

DOI: <https://dx.doi.org/10.18203/2319-2003.ijbcp20231122>

Original Research Article

## Analysis of fixed dose combinations of expectorants, antitussives, decongestants, antihistamines and mucolytics available in the Indian market for rationality and cost variation

Sathish Kumar B.\*, Rohan A., Naveen Gowda B.

Department of Pharmacology, Bangalore Medical College and Research Institute, Bengaluru, Karnataka, India

**Received:** 02 March 2023

**Accepted:** 01 April 2023

**\*Correspondence:**

Dr. Sathish Kumar B.,

Email: [sathish.nikhom@gmail.com](mailto:sathish.nikhom@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Background:** Aim of the current study was to analyze the FDCs of expectorants, antitussives, decongestants, antihistamines and mucolytics available in the Indian market for their rationality, cost, and dosage forms.

**Methods:** FDCs involving expectorants, antitussives, decongestants, antihistamines and mucolytics listed on Drug Today and Jan Aushadhi online portal were analysed for rationality according to the list of banned FDCs by CDSCO published on 01 Jan 2018. The FDCs with EADAM available in Jan Aushadhi online portal are compared with cost of different brands with same composition, strength and dosage form available in the Indian market as per the latest drug today. The cost ratio and percentage cost variation were calculated for each FDC.

**Results:** Out of total 340 oral formulations, 268 were liquid and 72 were solid formulations. 228 were Syrups, 67 were Tablets, 23 were Drops, 17 were Suspension and 5 were Capsules. Out of 47 banned FDCs, branded FDC with Ammonium chloride 50mg, Bromhexine 4mg, Dextromethorphan 5mg and Menthol in syrup form was still available for over-the-counter purchase and for online purchase with prescription. Percentage cost variation between branded and generic FDCs ranged from 99% for Terbutaline 2.5 mg and Bromhexine 8 mg to 1081% for Terbutaline 1.25 mg, Bromhexine 4mg, Guaiphenesin 50 mg and Menthol 2.5 mg.

**Conclusions:** One among 47 Banned FDCs was available at both online apps and drug stores. These irrational FDCs can be risk to human lives. The drug authorities need to tune the price of these FDCs as there is a huge percentage cost variation between generic and branded products.

**Keywords:** Fixed dose combination, Irrational drugs, CDSCO, Banned drugs, Jan aushadhi, Mucoactive

### INTRODUCTION

Medications that influence the properties of mucus and enhance secretion clearance are referred to as 'muco-active' drugs. This group includes expectorants and mucolytics. Expectorants help in increasing the volume of secretions and improve clearance of purulent secretions.<sup>1</sup> Mucolytics change the biophysical properties of secretions by degrading the mucin polymers, DNA, fibrin, or F actin in airway secretions, decreasing viscosity. Antihistamines

competitively antagonise histamine at H1 receptor and decreases sneezing, rhinorrhoea, conjunctivitis due to allergens but have no direct impact on nasal congestion. Decongestants relieve nasal congestion by decreasing nasal airway resistance. Antitussives act at peripheral and/or centrally and intended to reduce the frequency and/or intensity of coughing. 2 or more of these drugs involving EADAM (expectorants, antitussives, decongestants, antihistamines and mucolytics) are combined in a fixed ratio into a single dosage form called

fixed dose combinations (FDCs). FDCs are ideally aimed at gaining benefits of potentiating efficacy, reducing adverse effects, gaining pharmacokinetic advantage, better compliance or making treatment cheaper. All these can be achieved only if there is a rational combination of these drugs and if not rational, FDCs can cause more harm than benefit.<sup>2</sup> To address this, several initiatives have been launched.<sup>3</sup> On 01 Jan 2018, Central Drugs Standard Control Organization (CDSCO) published a list of 444 banned drugs including FDCs as they were found to be irrational<sup>3</sup>. 47 such FDCs were combinations of EADAM.<sup>4</sup> Cost of the drug is an essential factor influencing patient compliance with the treatment of disease. There are many branded formulations of the same drug supplied by the pharmaceutical industries with large difference in selling price.<sup>5</sup> Access to quality medicines is a crucial element of healthcare delivery. India despite being known as the "pharmacy of the third world," access to rational and cost-effective therapy remains an important issue. This study intends to do a reality check for the availability of these irrational FDCs with EADAM in the market and their cost variation compared to similar generic FDCs available in Jan Aushadhi stores.<sup>6</sup>

**METHODS**

This study was conducted in the department of pharmacology, Bangalore medical college and research institute. The study was exempted from ethical committee review because it did not involve any human or animal subjects. Data were obtained from the following sources: Drug Today January-April 2022, Jan Aushadhi product list from janaushadhi.gov.in accessed on Jan 2022. In this cross-sectional study, FDCs involving expectorants, antitussives, decongestants, antihistamines and mucolytics listed on most recently published Drug Today and Jan Aushadhi portal were analyzed for rationality according to the list of banned FDCs which were found to be irrational by CDSCO published on 01 January 2018. Cost variation analysis<sup>7</sup> was done by assessing the maximum and minimum costs of various branded preparations and generic preparations from Drug today and Jan Aushadhi portal respectively. This involved FDCs with Expectorants, Antitussives, Decongestants, Antihistamines and Mucolytics for ten tablets/capsules, or one unit of syrup, suspension, drops. Cost ratio and percentage cost variation were derived from the below data. Cost ratio is defined as the ratio of the cost of highest priced to the lowest priced formulations of the same FDC, in same strength, same dosage form, for the unit containing same amount of the FDC. Cost ratio gives valuable information on how many times is the cost of the most expensive FDC more than the least expensive FDC, for the drug considered for evaluation. Cost ratio between the maximum and minimum cost of the same drug manufactured by different pharmaceutical companies was calculated as follows:

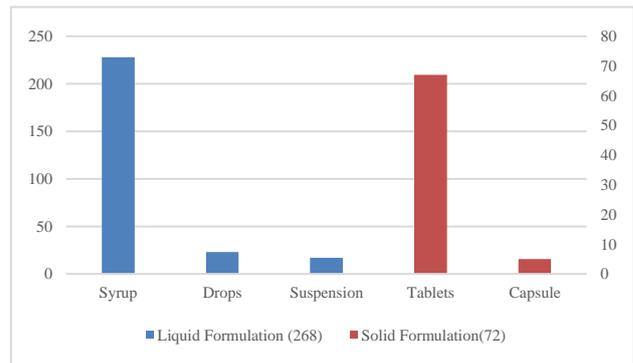
Cost ratio = Maximum cost/Minimum cost, Percentage cost variation (%) was calculated as follows:

$$\% \text{ Cost variation} = \frac{(\text{Maximum}-\text{Minimum cost}) \times 100}{\text{Minimum cost}}$$

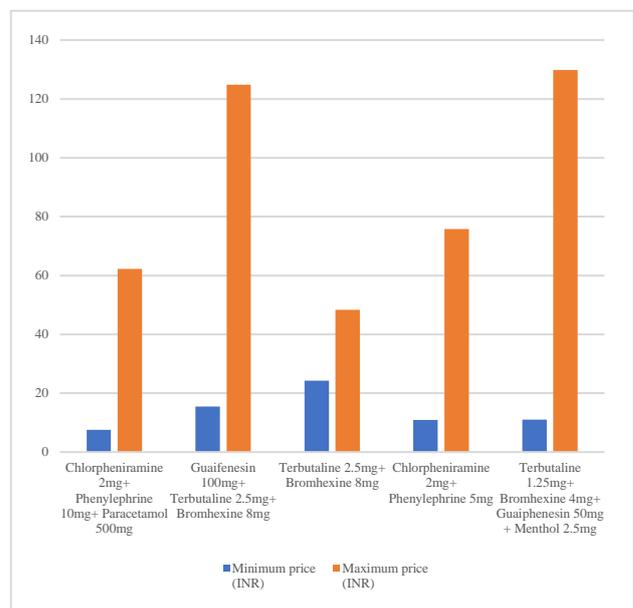
Data obtained were analysed using descriptive statistics.

**RESULTS**

Out of total 340 oral formulations, 268 were liquid and 72 were solid formulations. 228 were Syrups, 67 were Tablets, 23 were Drops, 17 were Suspension and 5 were Capsules (Figure 1).



**Figure 1: Dosage forms of commonly used expectorants, antitussives, decongestants, antihistamines and mucolytics.**



**Figure 2: Cost difference (minimum and maximum) of FDCs with EADAM.**

Out of 47 banned FDCs (Table 1), branded FDC with ammonium chloride, bromhexine, dextromethorphan and menthol in syrup form was still available for (OTC) over the counter purchase and for online purchase with prescription. Percentage cost variation between branded and generic FDCs ranged from 99% to 1081% (Table 2, Figure 4). 99% for Terbutaline 2.5 mg, Bromhexine 8 mg.

592% for Chlorpheniramine 2 mg, Phenylephrine 5 mg.  
705% for Guaifenesin 100 mg, Terbutaline 2.5 mg and

Bromhexine 8 mg. 722% for Chlorpheniramine 2 mg,  
Phenylephrine 10 mg and Paracetamol 500 mg.

**Table 1: Banned FDCs with EADAM.**

Banned FDCs with EADAM
Paracetamol+Phenylephrine+Chlorpheniramine+Dextromethorphan+Caffeine
Dextromethorphan+Levocetirizine+Phenylephrine+Zinc
Dextromethorphan+bromhexine+Guaifenesin
Paracetamol+Loratadine+phenylephrine+Dextromethorphan+caffeine
Dextromethorphan+chlorpheniramine+Chlorpheniramine maleate
Dextromethorphan+triprolidine+phenylephrine
Terpin hydrate+dextromethorphan+menthol
Dextromethorphan+phenylephrine+zinc gluconate+menthol
Bromhexine+Dextromethorphan+Phenylephrine+Menthol
Cetirizine+dextromethorphan+phenylephrine+zinc gluconate+paracetamol+menthol
Paracetamol+pseudoephedrine+dextromethorphan+cetirizine
Chlorpheniramine+Dextromethorphan+Phenylephrine+Paracetamol
Pseudoephedrine+Dextromethorphan+Cetirizine
Ambroxol+Terbutaline+Dextromethorphan
Dextromethorphan+Chlorpheniramine+Guaifenesin
Terbutaline+Bromhexine+Guaifenesin+Dextromethorphan
Dextromethorphan+Triprolidine+Phenylephrine
Paracetamol+Dextromethorphan+Chlorpheniramine
Dextromethorphan+ambroxol+guaifenesin+phenylephrine+chlorpheniramine
Cetirizine+Phenylephrine+Dextromethorphan+Menthol
Cetirizine+Acetaminophen+Dextromethorphan+Phenylephrine+Zinc gluconate
Cetirizine+Dextromethorphan+Zinc Gluconate+Menthol
Dextromethorphan+phenylephrine+ammonium chloride+menthol
Dextromethorphan+bromhexine+guaifenesin+menthol
Dextromethorphan+Phenylephrine+Guaifenesin
Dextromethorphan+Chlorpheniramine+Ammonium Chloride+Menthol
Chlorpheniramine+Dextromethorphan+Guaifenesin+Phenylephrine
Dextromethorphan+Paracetamol+Cetirizine+Phenylephrine
Dextromethorphan+Phenylephrine+Triprolidine+Menthol
Dextromethorphan+Phenylephrine+Bromhexine+Guaifenesin+Chlorpheniramine
Dextromethorphan+Phenylephrine+Guaifenesin+Cetirizine+Acetaminophen
Dextromethorphan+Cetirizine+Guaifenesin+Ammonium Chloride
Dextromethorphan+Ambroxol+Ammonium Chloride+Chlorpheniramine+Menthol
Dextromethorphan+Phenylephrine+Cetirizine+Zinc+Menthol
Bromhexine+Dextromethorphan
Dextromethorphan+Cetirizine
Dextromethorphan+Phenylephrine+Guaifenesin+Triprolidine
Ammonium Chloride+Bromhexine+Dextromethorphan
Cetirizine+Dextromethorphan+Ambroxol
Bromhexine+Dextromethorphan+Ammonium Chloride+Menthol
Dextromethorphan+Phenylephrine+Cetirizine+Paracetamol+Caffeine
Levocetirizine+Dextromethorphan+Zinc
Paracetamol+Dextromethorphan+Bromhexine+Phenylephrine+Diphenhydramine
Cetirizine+Dextromethorphan+Bromhexine+Guaifenesin
Acetaminophen+Guaifenesin+Dextromethorphan+Chlorpheniramine
Cetirizine+Dextromethorphan+Phenylephrine+Tulsi
Guaifenesin+Dextromethorphan

FDC with Bromhexine+Dextromethorphan+Ammonium Chloride+Menthol is still available on sale.

1081% for Terbutaline 1.25 mg, Bromhexine 4 mg,  
Guaifenesin 50 mg and Menthol 2.5 mg. Percentage cost  
variation between branded and generic FDCs ranged from

99% to 1081%. Cost ratios range from 1.99 to 11.81. Out  
of 340 oral formulations, 268 were liquid form and 72 were  
solid form. among the 268 liquid form there were 228

syrup, 23 drops, 17 suspensions. among 72 solid forms, there were 67 tablets form and 5 capsule forms.

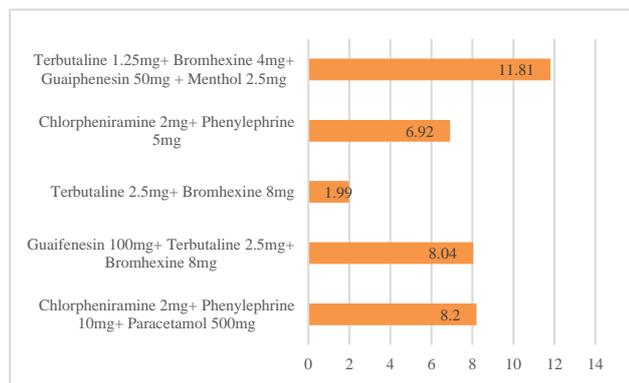


Figure 3: Cost ratio of FDCs with EADAM.

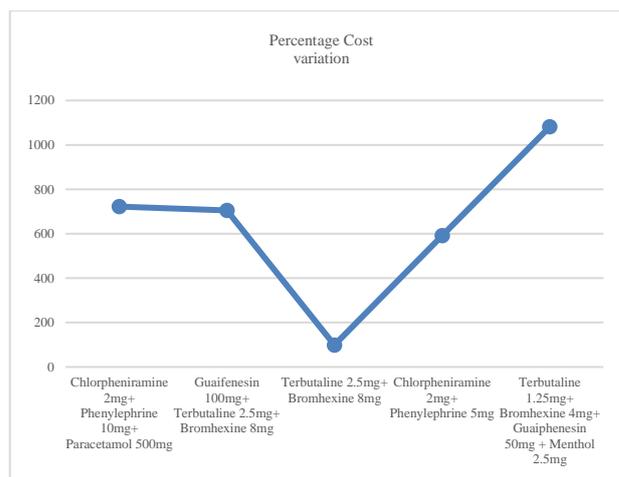


Figure 4: Percentage cost variation of FDCs with EADAM.

Table 2: Minimum and maximum cost, cost ratio and percentage cost variation of FDCs with EADAM.

Fixed dose combination	Minimum price (INR)	Maximum price (INR)	Cost ratio	Percentage cost variation
Chlorpheniramine 2mg+Phenylephrine 10mg+Paracetamol 500mg	7.57	62.2	8.22	721.66
Guaifenesin 100mg+Terbutaline 2.5mg+Bromhexine 8mg	15.51	124.8	8.05	704.64
Terbutaline 2.5mg+Bromhexine 8mg	24.26	48.3	1.99	99.09
Chlorpheniramine 2mg+Phenylephrine 5mg	10.95	75.8	6.92	592.24
Terbutaline 1.25mg+Bromhexine 4mg+Guaiphenesin 50mg+Menthol 2.5mg	10.99	129.8	11.81	1081.07

## DISCUSSION

Out of 340 Oral formulations, 228 were syrup and 67 were tablets making it to 87% of the total formulations available (Figure 1). Syrup seems to be the preferred dosage form by pharmaceutical companies. Studies have shown that the demulcent effect of syrup formulation adds to the positive effects of antitussive agents like Dextromethorphan.<sup>8</sup> Clinically, type of formulations has an important role in determining the outcome, adherence, and quality of life.<sup>9</sup> Syrup is convenient and easier to administer even in paediatric age group. A banned FDC as per CDSCO list of irrational FDCs published on 01 January 2018 with Ammonium chloride, Bromhexine, Dextromethorphan and Menthol in syrup form was found to be available for purchase over the counter and on the online stores. This FDC having components with expectorant, mucolytic and cough suppressant action may lead to an increased build-up of airway secretions without the ability to cough them out effectively leading to infection and inflammation and aggravating the clinical condition rather than treating it.<sup>1</sup>

A similar study in 2011 also showed that most of the antitussive preparations were irrational in Indian market and with no clinical benefits<sup>10</sup>. Studies have shown that Irrational FDCs are known to increase the risk of adverse events and associated morbidities.<sup>2</sup> This study findings showed a very high fluctuation in the minimum and maximum price of various FDCs manufactured by several companies across the different brands with Expectorants, Antitussives, Decongestants, Antihistamines and Mucolytics for ten tablets/capsules, or one unit of syrup, suspension and drops (Table 2, Figure 2). The cost ratio was also observed to be very high (Table 2, Figure 3). The percentage variation in the cost was ranging from 99% to 1081% with most of the commonly used FDC of various expectorants, antitussives, decongestants, antihistamines and mucolytics (Table 2, Figure 4). The price variation is because many pharmaceutical companies are involved in marketing same FDCs under different brand names without a proper system in place for registration of these FDCs. During the multiple covid waves, the demand for these FDCs increased further as cough was one of the common symptoms among patients with COVID infection. This imbalance between demand and supply

would have influenced sale of these drugs at a higher price further. The financial implications were severe particularly among poor, rural populations and impacted the accessibility to healthcare during covid waves.<sup>11</sup> Hence price control of these FDCs is of prime importance.

## CONCLUSION

Mostly rational FDCs were found to be available in Drug today according to the banned list of irrational FDCs notified by CDSCO except one with ammonium chloride, bromhexine, dextromethorphan and menthol in syrup form, available at both offline and online drug stores. With the menace of inappropriate over the counter sale of drugs, irrational FDCs can be risk to human lives. There is a wide variation in the prices of FDCs of EADAM from different brands and generics sold in Jan Aushadhi stores. The drug authorities need to tune the price of these FDCs.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Rubin BK, van der Schans CP, editors. Therapy for mucus clearance disorders, biology of the lung series. New York: Marcel Dekker; 2004.
2. Gupta YK, Ramachandran SS. Fixed dose drug combinations: Issues and challenges in India. Indian J Pharmacol. 2016;48:347-9.
3. Mohanta GP, Manna PK. Rational use of medicines - Indian perspective! Int J Risk Saf Med. 2015;27(1): S47-8.
4. List of banned FDCs. Available at: [http://www.cdsc.gov.in/opencms/en/consumer/list\\_of\\_banned\\_drugs](http://www.cdsc.gov.in/opencms/en/consumer/list_of_banned_drugs). Accessed on 25 January 2022.
5. Kamath L, Satish GR. Cost variation analysis of antihypertensive drugs available in Indian market: an economic perspective. Int J Pharma Sci Res. 2016;7(5): 2050.
6. Product and MRP list available at pharmaceuticals & medical devices bureau of India. Available at: [janaushadhi.gov.in](http://janaushadhi.gov.in). Accessed on 25 January 2022.
7. Ray A, Najmi A, Khandelwal G, Sadasivam B. A cost variation analysis of drugs available in the indian market for the management of thromboembolic disorders. Cureus. 2020;12(5):32-9.
8. Lejeune J, Weibel MA. Comparison of 2 antitussive agents in pediatrics. Rev Med Suisse Romande. 1990; 110:181-5.
9. Stewart KD, Johnston JA, Matza LS, Curtis SE. Preference for pharmaceutical formulation and treatment process attributes. Patient Prefer Adher. 2016;10:1385-99.
10. Roy V, Malhotra R, Tayal V, Bansal A, Gupta KS. Fixed-dose combinations for cough and common cold in India: An assessment of availability and rationality. Fundam Clin Pharmacol. 2011;25:258-66.
11. Singh, K, Kondal, D, Mohan, S, Jaganathan S. Health, psychosocial, and economic impacts of the COVID-19 pandemic on people with chronic conditions in India: a mixed methods study. BMC Public Health. 2021;21: 685.

**Cite this article as:** Kumar SB, Rohan A, Gowda NB. Analysis of fixed dose combinations of expectorants, antitussives, decongestants, antihistamines and mucolytics available in the Indian market for rationality and cost variation. Int J Basic Clin Pharmacol 2023;12:422-6.