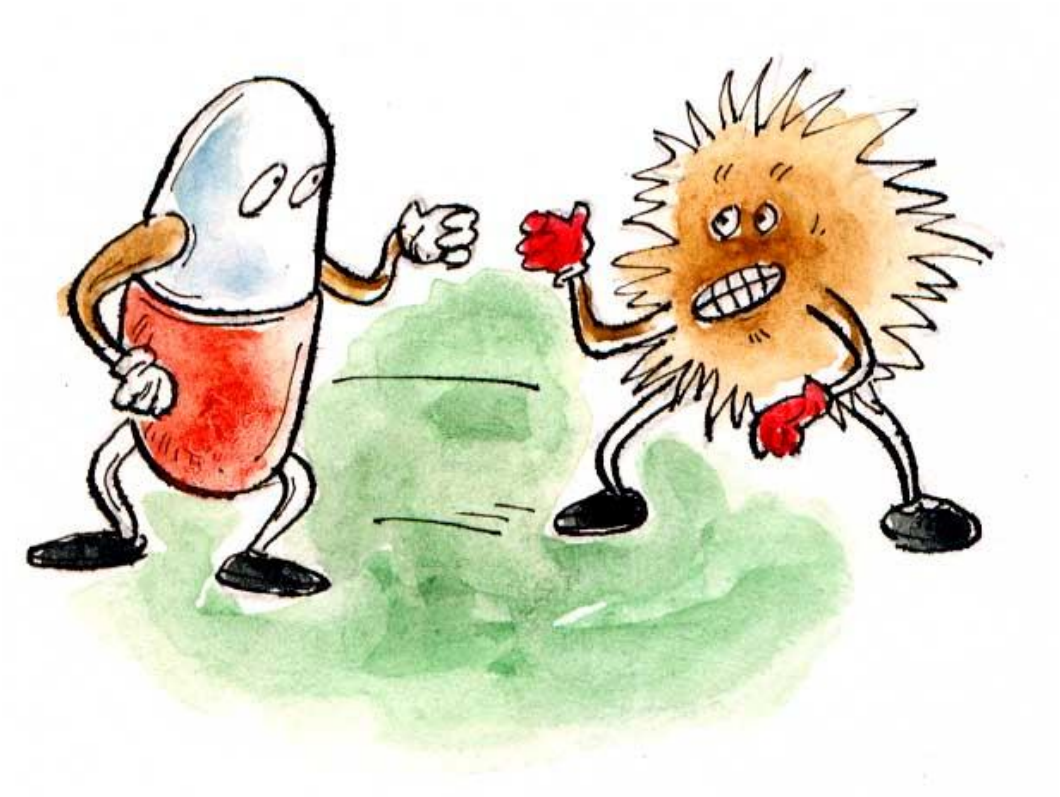
Report on research project

'Fixed-dose combination in India, inception – marketing – a study'



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Introduction

The Health Survey and Development Committee, popularly known as the Bhore Committee was set up by the Government of India in 1943, with Sir Joseph Bhore as the Chairman to survey the position and conditions of the health sector and health organizations functioning in the country, with a purpose of submitting recommendations for future development. The Committee, which had among its members some of the stalwarts of public health, met regularly for two years and submitted in 1946, its famous report – the Bhore Committee report, which runs in to four volumes.

The Committee put forward, for the first time, comprehensive proposals for the development of a national program of health services for the country. The Committee observed: "if the nation's health is to be built, the health program should be developed on a foundation of preventive health work and that such activities should proceed side by side with those concerned with the treatment of patients". Among of the important recommendations of the Bhore Committee was the integration of preventive and curative services at all administrative levels.

The Committee visualized the development of primary health centres in 2 stages

- As a short term measure, it was proposed that each primary health centre in the rural areas should cater to a population of 40,000, with a secondary health centre to serve as a supervisory, coordinating and referral institution. For each primary health centre two medical officers, four public health nurses, one nurse, four midwives, four trained dais, two sanitary inspectors, two health assistants, one pharmacist and fifteen other Class Four workers were recommended.
- a long term plan (also called the Three Million Plan) of setting up primary health units with 75 bedded hospitals for each 10,000 to 20,000 population and secondary units with 650 bedded hospitals, again reorganized around district hospitals with 2500 beds, was recommended.

Major changes in medical education were proposed, which would include three months' training in preventive and social medicine to prepare 'social physicians'.

Although the Bhore Committee recommendations did not form part of a comprehensive plan for national socio-economic development, the Committee's report continues to be a flagship national referral document, and has provided guidelines for the present national health planning modules in India.

In 1975, another significant committee, the Hathi Committee was appointed by the Government of India to analyze the existing Indian drug industry scenario, and the committee recommended a) a restricted list of essential drugs and suggested, that b)certain measures be implemented to ensure their production, and c) that a gradual shift be made from brand names to generic names, d) that price control measures be effected with the aim of making life-saving drugs and essential drugs affordable e) that

public sector should play a leading role in drug production and most importantly, f) certain drugs be reserved to encourage the growth of Indian drug companies.
The Committee also recommended elimination of irrational drugs, and decried the role played by MNCs, and recommended immediate dilution of foreign equity in drug companies up to 40% and progressively to 26%. It had, in fact recommended the nationalization of foreign drug companies. This was a visionary report.

(For more details please refer to the Hathi Committee, Report of the Committee on the Drugs and Pharmaceutical Industry, Ministry of Petroleum and Chemicals, Government of India, New Delhi, April 1975).
The Indian Patent Act 1970, enacted since 1972, recognized only process patent in pharmaceuticals, which helped the Indian Pharma Industry to grow to the tune of Rs. 750000 crore. Gradually India became the global hub for producing generic medicines and is serving a large population suffering from HIV/AIDS throughout the globe, especially in the African countries.

As a consequence of IPR regime, India also amended its Patent Act since 1st January 2005 and allowed Product Patent in Pharmaceuticals. Inspite of complying with the TRIPS obligations, pharma industrial houses wish to enjoy benefits of monopoly.Recently Pfizer has lost a case at Supreme Court where they have challenged DCGI & Govt. of India for granting generic version of Sorafinib tosylate.

Definition: Fixed-dose combinations are defined by WHO as "a combination of two or more active ingredients in fixed ratio of doses. This term is used generically to mean particular combination of active irrespective of the formulation or brand. It may be administered as single entity products given concurrently or as finished pharmaceutical products". [WHO technical report 929][1]

Drug Consultative Committee (DCC) opined that:
Fixed dose combinations (FDCs) should be allowed when (a) there is synergistic action of two or more drugs i.e. the combination acts to achieve a better therapeutic response than individual drugs alone or (b) when there is corrective action i.e. one drug acts to reduce the incidence and/or severity of adverse effects caused by the other or (c) when two or more molecules are normally needed and taken by the patient concurrently, provided the dosage of each drug does not need to be individualized or (d) when two or more drugs, if prescribed separately, may lead to non-ingestion of one of them adversely affecting the health of a patient. Even under such situations, care has to be taken to ensure that there are no adverse interactions between the combined drugs, that the pharmacological behaviour (absorption, duration of action, elimination) is not grossly different, that the withdrawal of one of the agents does not lead to withdrawal symptoms and in any event sub-therapeutic doses are never used.

Conversely medicines can not be mixed if side effects are additive or they belong to the same group with similar mode of action such as two NSAIDs.

Fixed-dose combinations are **appropriate** for:

- Convenience, with improved patient compliance. This is particularly appropriate when two drugs are used as constant dose, for a long-term, for asymptomatic combinations. The fewer tablets the patients have to take, more reliably will they use them, especially the elderly- who as a group receive more drugs because they exhibit multiple disease symptoms and afflictions.
- *Enhanced effect.* Single drug treatment of tuberculosis leads to emergence of resistant mycobacteria; this effect is prevented or delayed by using two or more drugs simultaneously. Oral contraception [with an estrogen & progesterone combination] is used for the same reason.
- Minimization of unwanted effects. Combining levodopa with benserazide or with carbidopa slows its metabolism outside the central nervous system so that smaller amount of levodopa can be used; this reduces adverse effect.

Fixed-dose combinations are **inappropriate**:

- When the dose of one or more of the component drugs may need to be adjusted independently. A drug with a wide dose range that must be adjusted to suit the patient response is unsuitable for combination with a drug that has a narrow dose range.
- If the time course of drug action demands different intervals between administration of the components
- If the irregularity of administration, e.g. in response to a symptom such as pain & cough, is desirable for some ingredient but not for others. [2]

The 16th list of essential medicines by WHO has only 25 FDCs out of total number of 329 medicines. The 2nd National List of Essential Medicines of India was published in 2003 has only only 13 FDCs out of 354 medicines. The details are as follows:

Name of the list	Number of FDCs	List of FDCs
WHO Essential Medicine List	25	1. Amoxicillin + clavulanic acid 2. artemether + lumefantrine 3. benzoic acid + salicyclic acid 4. efavirenz + emtricitabine + tenofovir 5. estradiol cypionate + medoxyprogesterone acetate 6. ethambutol + isoniazid 7. ethambutol + isoniazid + pyrazinamide + rifampicin 8. ethambutol + isoniazid + rifampicin 9. ethinylestradiol + levonorgestrel 10. ethinylestradiol + norethisterone 11. ferrous salt + folic acid 12. glucose with sodium chloride

		13. imipenem + cilastatin 14. isoniazid + pyrazinamide + rifampicin 15. isoniazid + rifampicin 16. lamividine + nevirapine + stavudine 17. lamividine + nevirapine + zidovudine 18. lamividine + zidovudine 19. levodopa + carbidopa 20. lidocaine + epinephrine (adrenaline) 21. lopinavir + ritonavir 22. neomycin sulfate + bacitracin 23. oral rehydration salt 24. sulphadoxine + pyrimethamine 25. sulfamethoxazole + trimethoprim
India Essential Drug List	13	1. Acriflavin + glycerin 2. Aluminium hydroxide + magnesium hydroxide 3. Benzoic acid + salicyclic acid 4. Sulfamethoxazole + trimethoprim 5. Ethinylestradiol + levonorgesterol 6. Ethinylestradiol + norethisterone 7. Lamivudine + zidovudine 8. Lamivudine + nevirapine + stavudine 9. levodopa + carbidopa 10. lignocaine hydrochloride + Adrenaline 11. Neomycin + bacitracin 12. Sulphadoxine + pyrimethamine 13. Thiacetazone + isoniazid

It has been quoted frequently that over 80000 – 100000 formulations are sold in the Indian market (though there is no comprehensive data base), most of them are FDCs, many of them having no pharmacological basis.

Drug licensing procedure in India

There has been an alarming increase in irrational FDCs in the recent past and the pharmaceutical companies manufacturing these FDCs are luring physicians to prescribe their products even when they are unnecessary for the patients.

As per the Drugs and Cosmetics [D & C] Act and Rules, Central Drug Standard Control Organization (CDSCO) is responsible for granting "New Drugs". FDCs which are new

in India, are also considered as "New Drugs" as per Rule 122E of Drugs and Cosmetics Rules as included in the year of 1999.

Rule 122E:
a. A drug, as defined in the Act including bulk drug substance which has not been used in the country to any significant extent (no clarification provided by the act - it is the prerogative of the Licensing Authority) under the conditions prescribed, recommended or suggested in the labeling thereof and has not been recognized as effective and safe by the licensing authority under rule 21 for the purposes claimed; provided that the limited use, if any, has been with the permission of the licensing authority.

b. A drug already approved by the Licensing Authority mentioned in Rule 21 for certain claims, which are now proposed to be marketed with modified or new claims, namely, indications, dosage, dosage form (including sustained release dosage form) and route of administration.

c. A fixed dose combination of two or more drugs, individually approved earlier for certain claims, which are now proposed to be combined for the first time in a fixed ratio, or if the ratio of ingredients in an already marketed combination is proposed to be changed, with certain claims, viz., indications, dosage, dosage form (including sustained release dosage form) and route of administration.

It also explained that all vaccines shall be new drugs unless certified otherwise by the Licensing Authority and a new drug shall continue to be considered as a new drug for a period of four years from the date of its first approval or its inclusion in the Indian Pharmacopoeia whichever is earlier.

All new drugs are required to comply with the provisions and requirements of Schedule Y for registration in India. However some relaxations have been granted for fixed dose combinations to be registered in India. For this purpose fixed dose combinations are categorized into the following four groups:

- **The first group** of Fixed Dose Combination (FDC) includes those in which one or more of the active ingredients are a new drug. Such FDC are treated in the same way as any other new drug, for both clinical trials and marketing permission.
- **The second group** of FDC includes those in which the active ingredients are already approved and marketed individually and are combined for the first time, for a particular claim and where the ingredients are likely to have significant interaction of a pharmacodynamic or pharmacokinetic nature For permission to carry out clinical trials with such FDCs, a summary of available pharmacological, toxicological and clinical data on the individual ingredients should be submitted, along with the rationale for combining them in the proposed ratio. In addition, acute toxicity data (LD 50) and pharmacological data should also be submitted on the individual ingredients as well as their combination in the proposed ratio. If clinical trials have been carried out with the

FDC in other countries, reports of such trials should be submitted. If the FDC is marketed abroad, the regulatory trials performed should be stated.

For marketing permission, the reports of clinical trials carried out with the FDC in India should be submitted. The nature of the trials depends on the claims to be made and the data already available.

- **The third group** of FDCs includes those which have received marketing approval, but in which it is proposed either to change the ratio of active ingredients or to make a new therapeutic claim. For such FDCs, the therapeutic rationale should be submitted to obtain permission for clinical trials and the reports of trials should be submitted to obtain marketing permission. The nature of the trials will depend on the claims to be made and the data already available.
- **The fourth group** of FDCs includes those whose individual active ingredients have been widely used for a particular indication for years, their concomitant use is often necessary and no claim is proposed to be made other than convenience. Also it must be a stable acceptable dosage form and whose ingredients are unlikely to have significant interaction of a pharmacodynamic or pharmacokinetic nature.

  If any drug does not fall under the ambit of a new drug, licenses could be issued by the State Licensing Authority.

Once a FDC is approved by CDSCO, it will continue to be a new drug and require approval from CDSCO for four years. After completion of four years the state drug controllers are entitled to approve such FDCs following the norms stipulated in the D & C Rules. But unfortunately a trend is prevailing in some of the states, where the provisions of the D & C Rules are not being followed, and FDCs, are being approved by regulatory authorities, which are "New Drugs" as per the definition under Rule 122E e.g. Maharastra FDA has approved an FDC of Nimesulide & Paracetamol without approval of DCGI and it was subsequently withdrawn due to public outcry.

Moreover, approval of FDCs by state drugs controllers hardly take into consideration, the scientific basis of combining more than one drug. Existing provisions in the D & C Rules are considered insufficient to ensure scientific evidence before approving any FDC.

In India if an FDC is approved in any state, the same could be marketed throughout the country. The company does not require any clearance from any other state where it is being marketed.

A primary analysis shows that from 2004 (June) to 2010 [August] more than 474 FDCs have been approved for marketing[3].

In September 2007 the Drug Controller General of India [DCGI] had circulated a notification declaring 294 FDCs as irrational.

The Confederation of Indian Pharmaceutical Industries [CIPI] moved the Madras High Court and received stay order on DCGI's directive against the 294 FDC drugs categorized into 'absurd', 'rejected', banned, and under examination. The CIPI was willing to withdraw the cases if the DGCI agrees to allow licenses to the 150 FDC drugs which were categorized as need further examination'.

The present DGCI list of unapproved FDCs contains 115 combinations.

Objectives:

- Procedure for approval of FDCs in India.
- To enlist irrational fixed-dose combinations available in Indian pharmaceutical market
- Availability of selected IFDCs in 3 major cities of West Bengal

Study team

The team consists of following persons:

- Dr. Mira Shiva – AIDAN
- Dr. C M Gulhati – Editor, MIMS
- Dr. Gopal Dabade - AIDAN
- Dr. Sajal Kumar Roy Choudhury – Director, Directorate of Drugs Control, Govt of West Bengal
- Dr. Subhash C. Mandal –Vice President– Indian Pharmaceutical Association
- Dr. Moitreyee Mandal, Lecturer in Pharmacy.
- Dr. Samaresh Bhattacherjee – Senior Program Officer, Child In Need Institute
- Dr. Punya Brata Gun – Secretary, Maitri Swasthya Kendra
- Ms. Sulagna Dutta, CDMU
- Mr. Sushanta Roy, CDMU

Methodology:

In our country the commercial formularies available are as follows:

- The Current Index of Medical Specialties [CIMS]
- Monthly Index Medicine Specialist [MIMS]
- Drug Today
- Drug Index

We used CIMS[4] as a reference for preparation of the list of IFDCs, because it is widely available and product listing is better here.

Besides listing of IFDCs from the commercial formulary, we consulted commercial formularies for availability of formulations which have been unapproved by DGCI [list of 115 combinations]. Certain pharma companies took this advantage, and by slight changes effected in the composition of the same brand, are selling the "new" product at higher prices. The interesting fact is that most of the combinations marketed by the companies are permitted by the State Licensing Authorities, which is in clear violation

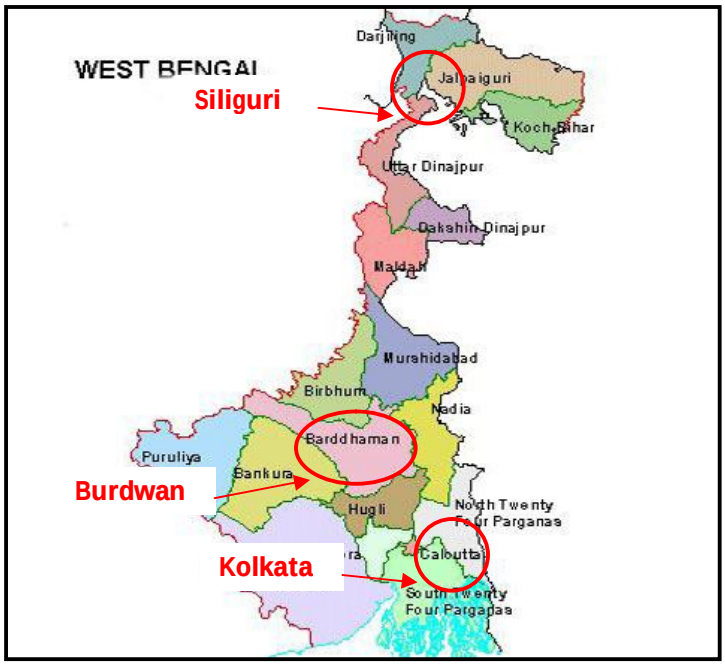
of the law in the first place. A careful study of commercial formularies for these 115 combinations, revealed that 52 combinations are absent in the commercial formularies. 13 combinations are multiple entries. 50 unapproved combinations are still listed in the commercial formularies. The pharmacological evidence of irrationality of these 50 combinations is annexed [**Annex 1**].

The availability of these 50 IFDCs in the commercial market was surveyed in 3 selected cities in West Bengal namely Kolkata, Siliguri and Burdwan. The map shows the position of the towns in West Bengal.

Besides these 50 combinations, we have also prepared lists of irrational combinations and corresponding brands of tonics, cough & cold preparations, vitamins, hematinics and oral hypoglycemic as they are widely used. We also surveyed their availability in the commercial market.

In Kolkata, we checked the availability of the above-mentioned formulations in 100 retail outlets, one each from each pin code, as the total number of pin codes in Kolkata is 100. In Burdwan, 35 retail outlets one each from 35 municipal wards were chosen, as the total number of municipal wards is 35. In Siliguri, 26 retail outlets one each from 26 wards were selected. Retail outlets were selected from the areas where a large number of customers visit the outlet e.g. near Hospitals, markets. etc.

We have also listed the IFDCs from top selling 60 brands in India.



Observation:

After careful observation of listed IFDCs in commercial formularies, it was found that 1356 FDCs which are supposed to be irrational and 4559 brands are listed. The details of IFDCs according to therapeutic categories are as follows: The annexure [**Annex 2**] will also give a clear picture about each combination and their respective brands.

Sl no	Therapeutic groups	Number of IFDCs	Number of brands
1	Gastrointestinal	169	670
2	Cardiovascular	108	526
3	Respiratory System	18	48
4	Central Nervous System	133	762
4	Musculo-Skelatal System	37	106
5	Anti-infective	80	472
6	Oncology	1	5
7	Genito-Urinary System	26	65
	Vitamins & Minerals	2	60
8	Supplements & Adjuvant Therapy	16	38
9	Eye	79	143
10	Ear & Mouth/Throat	42	75
11	Dermatologicals	196	394
12	Allergy & Immune System	28	73
13	Tonics	40	101
14	Cough & Cold preparations	167	494
15	Vitamin & Tonics	64	84
16	Hematinics	132	212
17	Oral hypoglycemics	18	231
	Total	1356	4559

From the DGCI list of 50 combinations, in Kolkata retail shops it was found that on an average 13 ($_{Max}$ 28 $_{Min}$ 7) combinations and 14 brands ($_{Max}$ 40 $_{Min}$ 7) are available in a shop. In Burdwan an average of 27 ($_{Max}$ 79 $_{Min}$ 5) brands and 26 ($_{Max}$ 21 $_{Min}$ 5) combinations are available in a shop. In Siliguri an average of 15 ($_{Max}$ 21 $_{Min}$ 7) brands and 8 ($_{Max}$ 10 $_{Min}$ 5) combinations are available in a shop. In Kolkata the most popular brands and combinations available in all the localities are as follows:

Sl no	Name of IFDCs	Popular Brand
1.	Aceclofenac + Paracetamol + Tizanidine	Zerodol – MR
2.	Diclofenac + Paracetamol + Serratiopeptidase	Enzoflam
3.	Nimesulide + Paracetamol + Serratiopeptidase	Sumoflam
4.	Glucosamine + Chondritin Sulphate +Vit C + Vit E + Manganese Sulphate	Rejoint
5.	Diclofenac + Paracetamol + Dextropropoxyphene	Buta-proxyvon
6.	Ca Pantothante, Vit B12, Folic Acid, Thiamine, Riboflavin, Pyridoxine, Niacinamide, Ascorbic Acid, Biotin, Elemental Zn	Becosules

Sl no	Name of IFDCs	Popular Brand
7.	Calcium pantothenate 12.5 mg, chromic chloride 65 mcg, cupric oxide 2.5 mg, folic acid 1 mg, manganese chloride 1.4 mg, niacinamide 50 mg, sodium selenate 60 mcg, vitamin A acetate 500 iu, vitamin B1 10 mg, vitamin B12 5 mcg, vitamin B2 10 mg, vitamin B6 3 mg, vitamin C 100 mg, vitamin D3 500 iu, vitamin E acetate 25 iu, zinc oxide 15 mg	A to Z
8.	Vit B1, Vit B2, Vit B6, Ca pantothenate, Nicotinamide, Vit C, Folic acid, Biotin	Polybion
9.	Ascoril	Terbutaline, Bromhexine, Guaifenesin
10.	Glipizide 5 mg, Metformin 500 mg	Glynase MF

The popular brand and combination available in Burdwan are as follows:

Sl no	Name of IFDCs	Popular Brand
1.	Paracetamol + Diclofenac Sodium + Magnesium Trisilicate + Chlorphenamine Maleate	Neurophen
2.	Aceclofenac + Paracetamol + Chloraxozone	Aceclo-MR
3.	Aceclofenac + Paracetamol + Serratopeptidase	Abdal-SP
4.	Diclofenac + Paracetamol + Chloraxozone	Adnac-MR, Dicoliv-MR
5.	Diclofenac + Paracetamol + Dextropropoxyphene	Buta-proxyvon
6.	Dicyclomine + Paracetamol + Dextropropoxyphene	Spasmo Proxyvon
7.	Ibuprofen + Paracetamol + Magnesium Trisilicate	Buwin Plus
8.	Nimesulide + Paracetamol + Serratiopeptidase	Nifen Plus
9.	Vit B1, Vit B2, Vit B6, Ca pantothenate, Nicotinamide, Vit C, Folic acid, Biotin	Polybion
10.	Alpha tocopheryl acetate 15 mg, ascorbic acid 75 mcg, biotin 150 mcg, boron 150 mcg, calcium pantothenate 10 mg, chromium 25 mcg, colloidal silicon dioxide 1 mg, copper sulphate 2 mg, cyanocobalamin 7.5 mcg, folic acid 1 mg, magnesium oxide 30 mg, manganese sulphate monohydrate 2.8 mg, molybdenum 25 mcg, niacinamide 50 mg, potassium iodide 150 mcg, pyridoxine hydrochloride 2 mg, riboflavin 10 mg, selenium dioxide monohydrate 70 mcg, thiamine mononitrate 10 mg, vitamin A acetate 5000 iu, vitamin D3 400 iu, zinc sulphate monohydrate 63 mg	Zincovit
11.	Terbutaline, Bromhexine, Guaifenesin	Ascoril

The popular brand and combination available in Siliguri are as follows:

Sl no	Name of IFDCs	Popular Brand
1.	Amoxicillin + Cloxacillin + Serratiopeptidase + Lactobacillus Sporogenes	Molox LBS
2.	Aceclofenac + Paracetamol + Chloraxozone	Nusaid-MR
3.	Aceclofenac + Paracetamol + Serratopeptidase	Aceclo-Sera, Fico-SP, Signoflam
4.	Aceclofenac + Paracetamol + Tizanidine	Zerodol-MR
5.	Aceclofenac + Paracetamol + Tramodol	Movon-PT
6.	Diclofenac + Paracetamol + Chloraxozone	Mobizox, Myospaz Forte
7.	Diclofenac + Paracetamol + Serratiopeptidase	Cuga Plus, Enzoflam, Kineto DP
8.	Dicyclomine + Paracetamol + Dextropropoxyphene	Spasmo Proxyvon
9.	Glucosamine + Chondritin Sulphate Vit C + Vit E + Manganese Sulphate	Rejoint
10.	Alpha tocopheryl acetate 15 mg, ascorbic acid 75 mcg, biotin 150 mcg, boron 150 mcg, calcium pantothenate 10 mg, chromium 25 mcg, colloidal silicon dioxide 1 mg, copper sulphate 2 mg, cyanocobalamin 7.5 mcg, folic acid 1 mg, magnesium oxide 30 mg, manganese sulphate monohydrate 2.8 mg, molybdenum 25 mcg, niacinamide 50 mg, potassium iodide 150 mcg, pyridoxine hydrochloride 2 mg, riboflavin 10 mg, selenium dioxide monohydrate 70 mcg, thiamine mononitrate 10 mg, vitamin A acetate 5000 iu, vitamin D3 400 iu, zinc sulphate monohydrate 63 mg	Zincovit
11.	calcium pantothenate 12.5 mg, chromic chloride 65 mcg, cupric oxide 2.5 mg, folic acid 1 mg, manganese chloride 1.4 mg, niacinamide 50 mg, sodium selenate 60 mcg, vitamin A acetate 500 iu, vitamin B1 10 mg, vitamin B12 5 mcg, vitamin B2 10 mg, vitamin B6 3 mg, vitamin C 100 mg, vitamin D3 500 iu, vitamin E acetate 25 iu, zinc oxide 15 mg	A to Z

We also tried to analyze 60 top selling brands[5]. Among the top 60 brands on an all – India basis, as on July, 2010 are IFDCs. We also try to find out the volume of business that these particular brand are doing in India. The details are as follows:

Therapeutic groups	Name of the brand	Turnover [Rs crore]
Cough & cold preparations	Corex	118.92
	Phensedyl Cough	203.05
	Sinarest	69.88
Vitamin tonics	Revital	155.07
	Becosules	142.66
Haematinics	Dexorange	145.35
Ayurvedic liver tonic	Liv-52	131.2

Therapeutic groups	Name of the brand	Turnover [Rs crore]
Antacid preparations	Digene	92.49
	Gelusil-MPS	71.57
Combinations meant for inhalation in bronchial asthma	Seroflo	90.20
	Aerocort	82.02
	Foracort	71.25
Combinations of analgesics	Combiflam	94.57
Miscellaneous	Zincovit	77.98
Combinations of Oral antidiabetic	Glycomet-GP	68.21
Combinations of vitamins with calcium	Shelcal	90.27

It was also note that in eastern India the top selling molecules introduced in eastern India and the volume of business are as follows[6]:

Sl no	Brand name	Composition	Turnover [crore Rs]
1.	Polybion-LC	Cyanocobalamin, Lysine, Nicotinamide, Pyridoxine	5.9
2.	Evion-Omega	Docosahexanoic Acid, Eicosapentaenoic Acid, Triticum Vulgare Oil, Vit E	3.7
3.	Polybion-SF	Cyanocobalamin, Dexpanthenol, Nicotinamide, Pyridoxine, Riboflavin, Thiamine	3.1
4.	Freeflex	Glucosamine, Chondritin	2.3
5.	B-Colen-NS	Copper Sulphate,Cyanocobalamin, Dexpanthenol, Lysine,Nicotinic Acid, Pyridoxine, Riboflavin, Thiamine, Zinc Sulphate	1.9
6.	Cefi-O	Cefixime, Ofloxacin	1.4
7.	Cefi-XL-D	Cefixime, Dicloxacillin Sodium	1.1

Discussion:

From the survey it has been revealed that in spite of being declared as irrational FDC by DCGI, a huge number of such products are available in the market. FDCs of NSAIDs and vitamins are more prevalent. A large number of products are available in India, which are banned almost all over the world, like Nimesulide. Products containing Serratiopeptidase, Glucosamine, Chondroitin Sulphate, whose therapeutic efficiencies are questionable, also figure in this list. Even recently banned in USA, New Zealand & Canada - Dextropropoxyphene is available in combination in India.

Availability is more in remote parts of the state. It may be due to low awareness level in the far flung areas in comparison to the capital city-Kolkata. Another reason may be relatively low vigilance in the remote places or it may be due to ineffective drug recall mechanism by the manufacturers from the market which are far from the capital.
It has also been noted that a large number of top selling products are irrational FDCs, both nationally and in the eastern part of this country.

It has been noted that a slow and lackadaisical judiciary system is also an important factor for adding more IFDCs in the large pool of IFDCs in Indian market. Cough syrups, Vitamin Tonics and Ayurvedic preparations figure among the highest selling products.

This study indicates low awareness level on irrational FDCs by the stake holders, inefficient recall mechanism by the manufacturers and a porous regulatory system.

Conclusion:

1. Identify and ban all irrational FDCs immediately.
2. Conduct time bound adequate clinical trials on borderline cases.
3. Approve only those which qualify in such trials and ban all other products

Scope of further action:

- Conducting extensive study throughout the country.
- Listing of IFDCs from all the commercial formularies
- Gathering pharmacological evidence against the IFDCs
- Lobbying with governmental agencies for withdrawal all IFDCs from market
- Campaigning to raise public consciousness

Reference:

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Photographs

National Consultation on IFDC project
November 19, 2010