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PARACETAMOL AND ITS COMBINATIONS IN INDIA –AN OVERVIEW

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ABSTRACT

Paracetamol the drug of choice for analgesic and as antipyretic which gain the fame by its availability of different dosage forms , wider clinical acceptance by casual easy go approach towards the people. After the India has signed in GATT agreement the flourishing of combination in the entire category of pharmaceutical started. Out of all combinational therapeutic range the Paracetamol has maximum number of combinations in India. The aim of the work is to collect the combinations which are available in Indian Pharma market and compile, sort out what are the other groups of drugs combined with Paracetamol to the public health. Apart from this compilation work we tried to find out what are the combinations which are banned by our drug control department to maintain and give the good therapeutic effect with minimal side effect for shake of nation's health policy.

KEYWORDS

Paracetamol, Acetanilide and Anti-inflammatory.

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INTRODUCTION

History of Paracetamol

The antipyretics commonly used at the time consisted of preparations of natural compounds such as cinchona bark, from which quinine is derived, or galenicals based on willow bark, the earliest source of salicylate. Cinchona bark became in short supply and cheaper, synthetic substitutes were needed[1]. The innovation of Acetanilide in 1886 and Phenacetin in 1887 both having analgesic and antipyretic effect

reduced the use of galenicals and advancements over quinine.

In 1893, another compound, now known as paracetamol, was noted also to have a prompt analgesic and antipyretic action[2]. In 1895, further work on this compound indicated that paracetamol might be present in the urine of patients who had taken phenacetin and in 1889; paracetamol was also shown to be a urinary metabolite of acetanilide[3]. In 1948 that Brodie and Axelrod established that paracetamol was a major metabolite of both phenacetin and acetanilide. This, and other work, led to the belief that the clinical effect of these two drugs was entirely due to rapid conversion in the body to paracetamol. This belief was supported by the observation that the analgesic and antipyretic effects of paracetamol were of the same order as those of its parent compound[4]. Some years later, it was shown that phenacetin had both effects in its own right and that paracetamol formation was not essential for its pharmacological action. However, because a very high proportion is converted to paracetamol during first passage through the liver, phenacetin it exerts a direct analgesic effect only at very high dose[5].

PARACETAMOL COMBINATIONS BANNED IN INDIA

1. Fixed dose combinations of vitamins with anti-inflammatory agents and tranquilizers- GSR N0 578[E] dated 23.07.1983[7].
2. Fixed dose combination of vitamins with analgesics GAR NI 578[E] dated 23.07.1983.
3. Fixed dose combinations of sedatives/ hypnotics /anxiolytics with analgesic and antipyretic –GSR NO 999 [E] dated 26.12.1990
4. Fixed dose combinations of Metoclopramide with systemically absorbed drugs except fixed dose combinations of metaclopramide with aspirin and paracetamol-GSR NO 395[E] dated 19.05.1999.
5. Fixed dose combination of oxyphenbutazone or phenylbutazone with any other drug –GSR NO 633[E] dated 13.09.1995[8].
6. Fixed dose combination of dextropropoxyphene with any other drug other than antispasmodic and or non-steroidal anti-inflammatory drugs-GSR NO 633 [E] dated 13.09.1995
7. Phenylpropalamine and its formulations for human use - GSR NO 82[E] dated10.02.2011
8. Limiting of acetaminophen [Paracetamol] in prescription combination products and giving box warning about its liver toxicity – recommendation of DTAB in its 59th meeting held on 24.06.2011 and also the manufacturers marketing combination products having more than 325 mg paracetamol should be asked to limit the paracetamol contents to 325 mg only in period of three years[9,10].

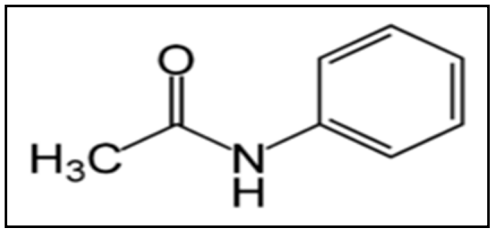
RESULTS AND DISCUSSION

From the above compilation work only paracetamol is having so many combinations with single drug and also with 5 combinations in India. The paracetamol is available with analgesic of opoid and NSAID, muscle relaxants, expectorant, antihistaminic, mucolytic, nasal decongestant, antacid, sedative and also available as with its one antidote.

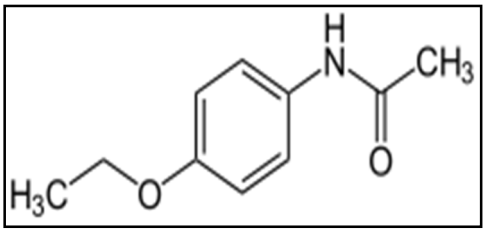
The market research we conclude that from the inception of paracetamol in analgesic and antipyretic drug of choice and wider combinations so much older and more side effect drug combinations completely gone out from the market. Still almost all Pharma companies are tried to find newer combinations for the health aspect of Indian population.

From the studies in the Indian pharmaceutical market this is only drug which is having wider range of therapeutic combinations and serve as a major drug in analgesic and antipyretic sector

STRUCTURE OF ACETANILIDE



STRUCTURE OF PHENACETIN



STRUCTURE OF PARACETAMOL

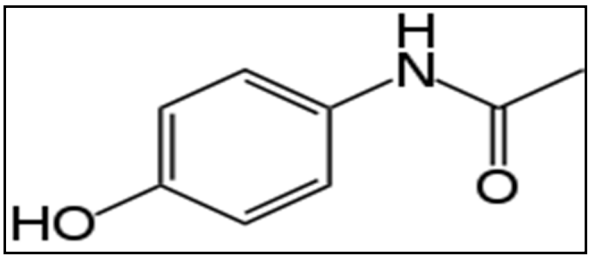


Table No.1: Paracetamol Brands First Marketed Companies

S.No	DOSAGE FORM	COMPANY	COUNTRY	YEAR
1	Elixir	Sterling Winthrop	United state	1953
2	Elixir for children	Mc Neil laboratories	United states	1955
3	500 mg tablet	Frederick steran& co	United kingdom	1956

Table No.2: Availability of Paracetamol Dosage Forms in India

SOLUTION 125 mg and 250 mg /5 ml	TABLETS FOR ADULT & KIDS 125 mg,250mg ,650 mg & 1000 mg	INFUSION 1000mg/100 ml
ELIXIR 125 mg /5 ml	INJECTION FOR IM AND IV 150mg/ml	DROPS 100mg/ml
SUSPENSION 125 mg/ 5 ml 250mg/ 5 ml 156.25 mg/ 5 ml	SUPPOSITORIES 80 mg & 170 mg	DISPERSIBLE TABLETS 125mg, 250 mg & 500mg
SYRUP 125mg/ml		

Table No.3: Paracetamol Combinations in India

CNS STIMULANT	ALKALANISING AGENT	ANTITODE	ANTIEMETIC	MUSCLE RELAXANT
Caffeine	Disodium hydrogen phosphate	Dl methionine	Domperidone	Methocarbomol
		Racemethionine	Metaclopramide	Chloroxazone
				Nebumetone

OPOID ANALGESIC	NSAID	NSAID	ANTI SPASMODIC
Codeine phosphate	Ibuprofen	Aceclofenac	Dicyclomine Hcl
Codeine sulphate	Diclofenac sodium	Piroxicam	Clidinium bromide
Dextropropoxyphene	Diclofenac potassium	Meloxicam	
Pentazocine	Nimesulide	Dexibiprofen	
Tramadol	Mefanamic acid	Phenylbutazone Propyphenazone Lornoxicam	

EXPECTORANT/NASAL DECONGESTANT/AH	OPOID ANALGEIS/ANTEMETIC	NSAID/ANTIHISTAMIC	MUCOLYTIC /ANTIHISTAMINIC
Phenylpropanalamine Dextromethrophene CPM	Tramadol Domperidone	Ibuprofen Promethazine	Bromhexine Guiapheneisine CPM
Dextromethorphan Pseudoephedrine CPM		Azatadine Pseudoephedrine	

NSAID +MUSCLE RELAXANAT	NSAID+MR+ANTACID	NSAID+ANTISPASMODIC	NSAID +ANTACID
Ibuprofen Methocarbomol	Diclofenac potassium Chloroxazone Mag trisilicate	Dicylomine Hcl Mefanamic acid	Diclofenac sodium Activated dimethicone
Aceclofenace Chloroxazone		Diclofenac sodium Dicylomine Hcl	Activated dimethicone
Diclofenac sodium Tizanidine		Dicylomine Hcl Dextropropoxyphene	
Diclofenac sodium Chloroxazone			

ANTI MIGRANINE/CNS STIMULANT	ANTIMIGRANINE/ANTIEMETIC	NSAID/VITAMIN	NSAID//OPOID ANALGESIC
Ergotamine tartrate Caffeine Belladonna dry extract	Ergotamine tartrate Caffeine Prochloperazine	Nimuslide Niacinamide	Aceclofenac Tramadol
			Diclofenac sodium Dextropopoxyphene
Dichlorophenazone Isometneptene mucate			

NSAID/CNS STIMULANT/NASAL DECONGESTANT	NSAID/ANTI-INFLAMMATORY ENZYMES	
Prophenazone Caffeine Ephedrine HCl	Ibuprofen Dextropropoxyphen Serratopeptidase	Nimesulide serratopeptidase
	Diclofenac sodium Serratopeptidase	Ibuprofen Dextropropoxyphene serratopeptidase
	Aceclofenace Serratopeptidase	

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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