

**EVERY HOUSEHOLD HAS IT.....
WHAT IS IT?...**

Paracetamol



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What is it??

WToday it is impossible to find a household whose members haven't used the Paracetamol tablets at one instance or the other!

What is this Paracetamol?

Paracetamol or acetaminophen chemically named N-acetyl-p-aminophenol, is a widely used over-the-counter analgesic (pain reliever) and antipyretic (fever reducer).

Paracetamol is classified as a mild analgesic. It is commonly used for the relief of headaches and other minor aches and pains and is a major ingredient in numerous cold and flu remedies. In combination with opioid analgesics, paracetamol can also be used in the management of more severe pain such as post-surgical pain and providing palliative care in advanced cancer patients.. While generally safe for use at recommended doses (1,000 mg per single dose and up to 4,000 mg per day for adults), acute overdoses of paracetamol can cause potentially fatal kidney, brain and liver damage and, in rare individuals, a normal dose can do the same.

Medical uses

Paracetamol is approved for reducing fever in people of all ages. The World Health Organization (WHO) recommends that paracetamol only

be used to treat fever in children if their temperature is greater than 38.5 °C (101.3 °F). Paracetamol has a well-established role in pediatric medicine as an effective analgesic and antipyretic.

Paracetamol is also used for the relief of pains associated with many parts of the body. It has analgesic properties comparable to those of aspirin, Available without a prescription; it has in recent years increasingly become a common household drug.

Prior to the usage of Paracetamol as antipyretic drugs; Aspirin was used to bring the fever down. Aspirin causes gastric irritation and it is a blood thinner and thus cannot be used in patients where coagulation (clotting of blood) is a concern, whereas the Paracetamol does not cause gastric irritation. However, Paracetamol does not help reduce inflammation like the Aspirin . Paracetamol is usually taken by mouth in tablet or capsule form. It is also available as liquids for children.

Safe recommended doses :

1,000 mg per single dose and up to 4,000 mg per day for adults.

Paracetamol usually comes in a 500mg tablet or capsule. It is also available in slow release (SR) 665mg tablets.

Liquid paracetamol is available for children. The dosage depends on the child's age.

The usual dose is 15mg per kg of body weight. Liquid paracetamol comes in different strengths so it is very important you check the strength to ensure that the dose above what is required is not administered.

The dose may need to be reduced if you have liver problems.

FREQUENCY OF DOSE:

Paracetamol can be taken when needed, that is when you feel the pain or have fever, or it may be taken regularly to manage persistent pain or fever. It is usually taken every 4 to 8 hours depending on the potency of the drug and the intensity of

pain or fever. It is preferable to ask your doctor or pharmacist if you are uncertain about how often to take your medicine.

Paracetamol can be taken safely during pregnancy or when breastfeeding.

Although paracetamol is administered to bring down fever in a patient, it is advisable to consult your doctor if the fever persists beyond 3 days and do further investigations to rule out any serious infection.

FEW DRUG CLASSIFICATIONS

- NSAID – Non steroidal anti inflammatory drug
- Therapeutic Action Classification
Analgesic - Relieves pain
Antipyretic - Brings down fever
- Schedule H -These are drugs which cannot be purchased over the counter without the prescription of a qualified doctor. The manufacture and sale of all drugs are covered under the Drugs and Cosmetics Act and Rules
- Schedule G – These are drugs to be used only under medical supervision
- OTC – Over the counter drugs. These can be procured without a medical prescription.

Paracetamol Is Classified As Aniline Analgesic As It Is Derived From Coal Tar And It Is An Analgesic.

Habitual use of paracetamol leads to decrease in threshold for pain in a person. This means that the endurance level for pain reduces in that person.

BEWARE!!! DO NOT HASTEN YOUR LIVER DAMAGE!!!!!!

Consuming more than 4 standard drinks at a time is likely to leave one with a hangover headache!! The most common thing to do is to pop a paracetamol tablet to get relief!!

This is very dangerous!! The liver damaging effect of alcohol is enhanced by taking the paracetamol tablet. Alcoholics or patients with liver damage should be careful about using Paracetamol.

COMPARATIVE TESTING

Comparative Testing is a formal process by which different brands of a product category are tested for :

- Conformance to minimum standards laid down by Bureau of Indian Standards
- Test how different brands exceed these standards or fall short
- An empirical analysis of what you get for your money
- Assess the inflated claims of manufacturers to see if consumers get what they pay for
- Relative performance of various brands
- The test results are published helping the consumer to make an informed choice.

CONCERT has undertaken this project of Comparative Testing for Southern Region under a grant from

Department of Consumer Affairs, Government of India. This is the second year and Concert will be testing 7 products and 3 services one of which is Paracetamol.

BRANDS CHOSEN FOR TESTING

Paracetamol Tablets:

1. Paracetamol Tablets 500 mg (Jan Aushadhi) made by IDPL (TN) Ltd, Chennai
2. Paracetamol Tablets 500 mg (Tamil Nadu Government supplies) made by Endoven Pharmaceuticals Pvt. Ltd, Hyderabad
3. P-500
4. Pacimal
5. Pyrigesic
6. Calpal
7. Crocin Advance
8. Paracip
9. Metacin

10. Acticin
11. Fepanil
12. Dolo 650
13. Pararite - 500
14. Paracetamol Tablets IP (500 mg) made by Locost, Baroda

Paracetamol – Paediatric Dosage:

1. Calpal 250 mg Oral Suspension
2. Crocin Oral Suspension
3. Fepanil 250 Oral Suspension
4. Lotemp Oral Suspension
5. Dolopar 250 Oral Suspension
6. Paracip 250 Oral suspension
7. P - 250 Oral Suspension

PARAMETERS TESTED were as per the standards prescribed in the INDIAN PHARMACOPEIA

1a) Labelling

Mandatory labelling Requirements of OTC Drugs in India

Drugs and Cosmetic Rules 1945 (manner of labelling) mandates the following minimum information to be put on the label of all OTC medicines:

- a. Generic and Trade name
- b. Net contents and content of active ingredient
- c. Date of manufacture
- d. Date of expiry
- e. Name and address of manufacturer including manufacture and the license number
- f. Batch number, manufacture and expiry date
- g. Maximum retail price
- h. Warning legend
- i. Directions for use/Dosage
- j. Net quantity
- k. Storage condition

1b) Warning Legend

Paracetamol should carry the warning – Overdose causes Liver Damage



2. QUALITY

(i) Identification Test is carried out to ascertain the identification of the active ingredient. This is a preliminary test done to ascertain the presence of the active ingredient and to ensure that a low cost isomer (same chemical composition but different molecular structure) which is ineffective, is not added.

(ii) Aminaphenol Test is done to ensure the purity of the active ingredient and it is an indication of the absence of impurity. It also helps determine the impurity profile if present.

(iii) Relative substance Test is done to identify and quantify the active ingredient. This is done using TLC or Thin layer Chromatography and comparing the result of the sample with the standard.

(iv) Uniformity of contents (weight) indicates that the formulation manufactured is uniform in terms of its content of active ingredient in all the packs. For instance if a strip of

10 tablets weighs 10gms then each tablet should weigh 1gm if there is uniformity of weight.

This test ascertains that all the tablets weigh 1gm each and the individual tablets are not packed in varying weights.

To ascertain this, 20 tablets are weighed on an electronic scale and the average weight is determined and the % deviation is recorded.

3. POTENCY AND EFFICACY

(i) Dissolution Test is carried out to determine the compliance with the dissolution requirements. It is an indication for efficacy and potency of the drug. If the drug is not dissolved, it will not be absorbed and hence will not have the desired effect.

(ii) Assay is an assurance that the formulation contains the quantity of active ingredient as claimed on the label. It is an indication of the efficacy/ potency of the drug and helps in therapeutic monitoring. The assay range is as indicated below.

Tablets

< 95% – Fail - 0

95% – minimum – 2

> 95% – <100% – 3

100% to 105% – 4

Suspensions

<90% – Fail – 0

90% – 95% – 2

95% – <100% – 3

100% – 110% – 4

Assay reading is a clear indication of quality and efficacy

As per Indian Pharmacopeia (IP) presence of 95% of the active ingredient is sufficient to meet the statutory requirement. Thus the drug which has a lower assay reading has compromised on the quantity of the active ingredient used thus bringing down the efficacy; more the active ingredient more effective is the drug.

A drug with an assay reading of 95% will contain 95% of the active ingredient and a drug with 110% assay reading contains 110% of active ingredient. 10% excess of the active ingredient is used in the manufacturing.

The Assay results for the various brands are tabulated below

TABLETS – Range 95 - 105%

BRAND NAME	ASSAY %
Jan Aushadhi supply (IDIMOL)*	97.97
Tamilnadu Government supply(Endoven)*	96.89
Calpol	98.70
Crocin Advance	98.37
Paracip 500*	99.64
Metacin	98.05
P -500	99.60
Pacimol	99.91
Acticin	97.00
Pyrigesic	99.54
Fepanil	99.36
Locost*	98.39
Dolo – 650	101.27
Pararite - 500*	101.11

*Generic- The branded drugs identified as generic by the pharmacists

ASSAY RESULTS – SUSPENSION (Range 90 - 110%)

Brand Name	Paracip	Dolopar	P-250	Calpal	Fepanil	Lotemp	Crocin
Assay (%)	93.7	100.45	101.25	103.48	99.5	99.67	101.83

Scoring and Rating for Paracetamol Tablets

Brand Name	Labelling	Quality	Efficacy/ Potency	Total score by different Weightage(%)
Jan Aushadhi supply (IDIMOL)*	Good	Good	Fair	75.00
Tamilnadu Government supply(Endoven)*	Fair	Good	Good	82.78
Calpol	Good	Good	Good	85.00
Crocin Advance	Fair	Good	Good	82.78
Paracip 500*	Good	Good	Good	85.00
Metacin	Good	Good	Good	85.00
P -500	Good	Good	Good	85.00
Pacimol	Good	Good	Good	85.00
Acticin	Good	Good	Good	85.00
Pyrigesic	Good	Good	Good	85.00
Fepanil	Good	Good	Good	85.00
Locost*	Good	Good	Good	85.00
Dolo – 650	Good	Good	V.Good	90.00
Pararite - 500*	Good	Good	V.Good	90.00

***Generic - The branded drugs identified as generic by the pharmacists**

SUSPENSION

Brand Name	Labelling	Quality	Efficacy / Potency	Total score by different weightage (%)	Price (MRP in Rs) 60ml
Paracip	Good	Good	Fair	70	35
Fepanil	Good	Good	Good	80	35.00
Lotemp	Good	Good	Good	80	50.80
Dolopar	Good	Good	V. Good	90	34
P - 250	Good	Good	V. Good	90	35.10
Calpal	Good	Good	V.Good	90	35.75
Crocin	Good	Good	V.Good	90	33.73

SCORING METHODOLOGY

TEST	RESULT	SCORING
QUALITY		
Identification	Fail/ Pass	0/2
4 Aminophenol test	Fail/ Pass	0/2
Relative substance	Fail/ Pass	0/2
Uniformity of weight	Fail/ Pass	0/2
EFFICACY/POTENCY		
Dissolution(only for Tablets)	Fail/ Pass (Range 0 to 4)	0/4
Uniformity of weight	Fail/ Pass	0/2
Assay*	Fail/ Pass (Range 0 to 4)	0/4
LABELING		
Label as per act	Fail/ Pass	0/2
Warning Legend	Yes/No	2/0

*Assay range and scores are as indicated in the assay table for Tablets and Suspensions

Weightage:

Labelling = 20%

Quality = 30%

Efficacy and potency = 50%
while rating the drug.

OBSERVATIONS AND RECOMMENDATIONS

Paracetamol suspension is sold under the brand names

Crocin Suspension

Lotemp

Fepanil 250

Calpol 250

P - 250

Indicate different pharmacopeial name like acetaminophen oral suspension as in USP (United States pharmacopoeia) , Paracetamol oral Suspension BP as in BP (British pharmacopoeia).

- As per the Drug and Cosmetic Act, the generic name given in IP Standard is Paracetamol suspension. The IP licensing authority can insist that the Generic name should be same as the Pharmacopeia name given in the IP Standards.
- **Crocin Advance**
As per Rule 97 of the Drugs and Cosmetics Act, the generic name should be indicated in a more conspicuous manner on the label

than the brand name The label of Crocin Advance does not give the generic name prominently as mandated by the Act.

- pH for paracetamol suspension is a vital factor in Stability of the formulation and on its absorption. IP does not specify this parameter. It is specified in USP. We recommend considering inclusion of specification for pH value in IP standards .
- Jan Aushadhi supplies IDIMOL brand made by IDPL, Tamil Nadu. This has passed the Dissolution Test only in S₂ stage; this indicates that the formulation needs improvement.
- Paracip brand of suspension made by HSN International, Hardwar, and marketed by CIPLA, Mumbai tested 93.7% assay content; this is closer to lower limit of 90% specified in IP for suspensions.

As mentioned earlier Assay is an assurance that the formulation contains the quantity of active ingredient as claimed on the label.

Paracetamol is a simple and stable formulation and the Indian Pharmacopoeia allows up to a minimum of 95% assay content. Manufacturers use this range (95% – 100%) in the specifications and make these products just to satisfy the lower limit thus qualifying for many

Government tenders. The Assay range should be increased to 100 - 105% to ensure the quantity of the active ingredient is not compromised.

The table below indicates the price per tablet which starts from 0.24 paisa and goes up to a maximum of Rs 2/- per tablet which is almost 8 to 9 times the price of the lowest brand listed.

Price per Tablet

BRAND NAME	Price (Per Tablet) in Rs
Jan Aushadhi supply (IDIMOL)*	0.24
Locost*	0.44
Pararite - 500*	1.05
Paracip 500*	1.10
Metacin	1.12
P -500	1.20
Calpol	1.21
Pacimol	1.21
Acticin	1.25
Fepanil	1.29
Pyrigesic	1.30
Dolo – 650	1.93
Crocin Advance	2.00

Why does the price of the tablets vary so much?

What are generic and branded drugs?

Is there a difference in quality between the generic and branded drugs?

What is patenting of drugs? Why is it done?

The answers to these questions helps a consumer to make a right choice as follows:

When a pharmaceutical company discovers a new drug to treat or prevent a condition or disease, they put it through a series of clinical trials in order to gain approval for marketing from the Medicines and Healthcare products Regulatory Agency. If the clinical trial results show that the new drug is safe and effective for the treatment of a particular condition,

the regulatory authorities approve the drug and give a licence. The company then has exclusive rights to market the medicine for the licensed uses for a certain period of time, usually about 10 to 12 years. This is known as a patent, and allows the drug company to recover the costs of research and development of the new medicine, before other drug companies are allowed to produce it as well.

Once a patent expires, other drug companies then have the right to manufacture and market the generic drug. However, they must market it under a different brand name, or under its generic name. Then the cost of the drug will be reduced due to open competition and the company which originally patented the drug has recovered all the expenses incurred in developing the drug.

In India however there were no patent laws till 2005 which meant that anyone could replicate any drug in India without legal ramifications. This led to the trend of branded generic drugs.

Generic name: a generic name that is the active ingredient of the medicine; drugs which have the same chemical composition as branded drugs are sold under their chemical name.

In India, if you go to the pharmacy seeking a generic paracetamol, the pharmacist will hand you a strip of paracip or pararite. This will leave you

wondering if it is truly generic! Since as per the definition a generic drug should be sold by the chemical name, i.e as Paracetamol.

Such drugs are called "Branded Generic drugs." This is an oxymoron (figure of speech which combines contradictory terms), but this is the way the Indian Pharmacists identify the generic paracetamol

The generic drugs without any brand names are packed in thousands and not individually. These are meant for hospitals and dispensaries. In our country the common man has access only to branded Generic drugs.

BRAND NAME OR TRADE NAME

It is the trade name the manufacturer gives to the medicine. It is chosen by the manufacturer usually on the basis that it can be easily pronounced, recognised, or remembered. For example, paracetamol is a generic name.

Calpol, Crocin, Dolo, etc. are the brand names or the trade names of the paracetamol given by different manufacturers

When a doctor is writing a prescription, or a consumer is buying an over-the-counter medicine, they have a choice between a branded medicine and the generic version of that medicine. Generic medicines are sometimes cheaper than brand-name medicines, but the active ingredient



(the ingredient that produces the therapeutic effect of the medicine) is the same in both.

Medicines also contain inactive ingredients, which are used to formulate the active ingredient into a tablet, liquid, cream or other preparation. These inactive ingredients are called excipients, and different manufacturers do not always use the same ones when formulating their product.

This is the reason why medicines containing the same active ingredient, but made by different manufacturers, may vary in appearance.

The excipients used may create small differences between them, such as in colour, or the amount of time it takes for a tablet to dissolve in the gut and be absorbed into the bloodstream, but these differences are rarely significant, which is why generic and branded medicines are (with a few exceptions) interchangeable.

If the doctor has prescribed a medicine by its brand name, the pharmacist will dispense that brand. However, if a medicine has been prescribed by its generic name, then the pharmacist can dispense whatever version of the medicine they have available, because each version will have the same therapeutic effect, regardless of whether one manufacturer makes the tablets a different shape or colour.

Generic prescribing helps in lowering the medicine cost. Sometimes we will seek a particular medicine, because we find that size and shape of tablet easier to swallow, or because it is a different colour from your other medicines and stops you getting confused between them, that your pharmacist should normally be happy to always give you that version.

DOCTORS CANNOT ALWAYS PRESCRIBE GENERIC MEDICINES

There are a handful of medicines that a doctor must prescribe by the brand name only.

Because different brands of these medicines may differ significantly in the way they are absorbed. If a different brand than usual is taken, the blood levels of the active ingredient could stray outside the required therapeutic range. If the amount in the blood becomes too low, the effect of the medicine may be lost; if the amount in the blood becomes too high, there may an increased chance of side effects.

E.g:

Modified-release theophylline for asthma, e.g Nuelin SA, Slo-phyllin, Uniphyllin continus

Modified-release aminophylline for asthma, e.g Norphyllin SR, Phyllocontin continus

MORE ABOUT GENERIC DRUGS

- Generic drugs are sold everywhere including your local chemist. To buy them one simply has to ask for the generic version of a branded drug though there may not be a generic form for all medicines.
- Government had set up a scheme called Jan Aushadhi whose purpose was to set up generic drugstores around the country.
- Doctors and chemists have the impression that the generic medicines are less effective. In fact some doctors avoid prescribing generic drugs as far as possible and even go to the extent of handing out free samples of branded drugs to patients who cannot afford branded medicines.
- Doctors also aren't aware about their availability due to lack of advertising and marketing.

Our test results show that many generic (brands) are as good as the branded ones

- Mindset of a person is that costlier the medicine more effective it will be! Since the generic drugs are cheap, people who can afford branded drugs don't buy them believing them to be of inferior.
- An opinion lingers that the private doctors would never hand out generic drugs because there are no kickbacks or incentives involved from pharma companies.
- There's a need to strengthen the Jan Aushadhi scheme and break down the doctor-big pharma nexus.

READING THE LABEL AND USING THE MEDICINE AS PER THE DIRECTION IS VERY ESSENTIAL FOR THE MEDICINE TO BE EFFECTIVE.

Sometimes, special directions for use are displayed on the label.

METHOD OF ADMINISTRATION

Some drugs produce the required therapeutic action only when they are administered through the particular route. For example, insulin, the anti-diabetic drug, should be administered subcutaneously, (by injection) as it is degraded by the enzymes in

the gastro-intestinal tract if it is administered through the oral route.

- **i.v/i.m.:** only for injections.
- **Oral:** for the drugs which can be administered through mouth.
- **Sublingual:** for drugs which should be placed under tongue.
- **For external use only :** For drugs meant for external use (should not be taken internally) for example, creams, gels, etc.
- **For nasal use only :** for drugs for inhalation through the nose.

Special instructions

Shake well before use - For suspensions like antacids (Gelucil). Suspensions have a tendency to settle at the bottom of the container. So, if it is not mixed properly, the body will not be getting proper amount of active ingredients for the therapeutic action.

Keep out of reach of children

Sugar-coated and beautifully coloured tablets/capsules are available - for example iron tablets. Children may mistake them for candy, so they must be stored out of reach of children. (If they are ingested in large numbers, it may lead to drug toxicity.)

Storage conditions

Storage conditions should be

recommended on the label (example "Keep in a cool, dry place") to maintain drug stability – i.e, to prevent contamination and as far as possible deterioration. It may be necessary to control elements such as temperature, moisture and light. If not stored properly, the medicine may expire well before the expiry date.

- Cold – 2-8°C
- Cool – 8-25°C
- Room temperature – Temperature prevailing in a working area
- Warm – 30 - 40°C
- Excessive heat – above 40°C
- Ointments should be kept below 30°C. Do not freeze.

Protection from freezing

It is indicated where there is a risk of breaking the container or where freezing leads to loss of strength or potency.

Not to be refrigerated

For example, soft gelatin capsules should not be refrigerated.

Protection from light

Store in a dark cupboard or use a light-resistant container.

Physician's sample – not to be sold

The label of sample drugs should display this. Sample drugs are not meant for sale.

Dosage as directed by the physician

The dose of a drug or the time interval between the doses is never increased or decreased unless directed by the physician. In most situations, drugs are administered in such a way as to maintain a steady state of drug in the body. The extent to which patients follow the instructions of doctor on medicine is called adherence or compliance.

It is often found that the patients do not follow or fail the dosage schedule prescribed for them. Non-adherence can worsen the quality of life.

For example, missed doses of medicines of heart problems may lead to more complications.

In the case of antibiotic therapy, missed doses of medicines are not only the problem of individual patients but are a global threat. The drug becomes ineffective at the moment and also ineffective permanently due to the development of new strains of bacteria which is capable of being drug resistant. The result is new powerful drugs have to be developed and introduced to get a germ-killing effect.

Try to develop a habit to observe the label of each and every drug. This will help you in proper usage and storage of drugs. If in doubt , ask your pharmacist for help.

Medicines are an integral part of life. Awareness should be created in the public to observe the

drug label for safe and effective use of medicine. For that, it is important to understand what is

displayed in the label of a drug that has certain identifying information.

Read label carefully for the following:

Expiry date

Dosage

Warning

Method of administration

Storage conditions

Next time when you buy medicines please ask the pharmacist to give you the generic medicine, if available.

Remember the generic drugs we are referring to are those brands identified as generics by the pharmacist.

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