Original Articles

New drugs in India over the past 15 years: Analysis of trends

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ABSTRACT

Background. New drugs are appearing in the Indian pharmaceutical market every day. To study the trends we analysed the pattern of new drug approvals and introductions in India over the past 15 years (1988–2002).

Methods. Lists of new drugs approved by the Drugs Controller General of India, released half-yearly, were obtained and entered into a computer database. Additional information, such as anatomical therapeutic chemical coding, availability status till 31 December 2002 and source were added to this database before analysing overall time trends and the situation in individual therapeutic categories.

Results. Excluding unrecognized and compound formulations and 28 veterinary products, 396 drugs were approved for clinical use during this period. Of these, 315 have also been launched in the market and 5 were subsequently withdrawn. Nervous system–related drugs accounted for the largest number of approvals (82), followed by antimicrobials (73) and cardiovascular drugs (57). Five new antimalarials have emerged but other tropical diseases have been mostly ignored. Eleven vaccines have been added.

Conclusion. There has been a sharp spurt in the annual number of approvals and introductions. The proliferation of brands and fixed–dose combinations has kept pace with the introduction of new molecules. Unfortunately, most new drugs are not major therapeutic advances. In the context of this rapid proliferation, meeting the information needs of prescribers, establishing an effective nationwide pharmacovigilance system and reorienting the focus of pharmacology education—from information provision to development of self-learning and critical judgement skills—are some issues for concern.

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INTRODUCTION

The past few decades have seen major advances in the various sciences contributing to the pharmaceutical industry such as pharmacology, biochemistry, synthetic and combinatorial chemistry, genetics, molecular biology, biotechnology, etc. Nowadays, potential drug targets are first identified, their DNA and amino acid sequences determined, their three-dimensional structure and stereochemistry mapped out in minute detail, and then a suitable designer ligand matching the above details synthesized. The mutual fit of the two is assessed and fine-tuned to perfection by molecular manipulation. New chemical entities can now be produced at an unprecedented rate.

Inevitably, this has led to the worldwide ushering in of new drugs, making it difficult to keep pace with these developments, be it as a doctor, student, academician, or researcher. Arguably, this scenario is a blessing, in that it offers better or safer treatment options to the prescriber, and brings down the price for the patient in the face of fierce competition. Others view it as a disturbing trend, as it coerces practitioners to prescribe fancier, sometimes more risky and often more expensive, therapeutic alternatives, without any real therapeutic advantage.

The Indian pharmaceutical industry has also developed remarkably. It is now one of the largest among the developing countries, with an annual turnover of more than Rs 200 billion. With new drugs being introduced in the Indian market at an astonishing pace, we considered it worthwhile to study the pattern of drug approvals and their subsequent introduction in India over a 15-year period (1988–2002).

METHODS

The Drugs Controller General of India, New Delhi, releases a list of new drugs approved for marketing in India every 6 months; the list specifies the names of the molecular entities, pharmacological classification/indication for use and date of approval. These data were entered into a Microsoft Access database. Additional information was added to this database, including the anatomical therapeutic chemical (ATC) classification maintained by the WHO,1,2 the current availability status in the Indian market after consulting commercial drug formularies,3–5 availability as fixed-dose combinations (FDCs) with other drugs, the likelihood of being used predominantly in a hospital setting, relation to major or emergent public health problems in India, and abuse liability. For ATC coding, 5-character alphanumeric codes were assigned, which adequately signified the group to which a drug belonged, all the close congeners having similar coding, without the need for specifying the full 7-character code unique to each drug. For new drugs that also exist in the strictly regulated pharmaceutical market of the USA, the date of approval of the new molecular entity (NME) by the United States Food and Drug Administration (US FDA) (available at http://www.fda.gov/cder) was entered in a separate column, if such approval occurred within the past 15 years, i.e. 1988–2002.

It was decided a priori that the following types of products would be excluded from the current analysis: (i) FDCs (except piperacillin+tazobactam and DPT–Haemophilus influenzae type B combined vaccine); (ii) combinations of existing products with b–cyclodextrin (piroximic, tenoxicam, nimesulide, domperidone, rofecoxib, silymarin, are currently available as b–cyclodextrin...
combinations); and (iii) novel dosage forms of existing drugs, e.g. hydrocortisone acetate rectal foam, proprietary oral release formulations, or change of formulation of existing compounds, e.g. levonorgestrel 750 mg, nicotinic acid 375 mg sustained release (SR), etc. Of the original list of 450 drugs obtained from the Drugs Controller’s office, 4 entries (viz. polyvinyl alcohol + povidone iodine + chlorbutanol, piroxicam with b-cyclodextrin, ciprofloxacin 1 g SR and mesalazine SR) warranted exclusion from the analysis by the above criteria.

Five drugs were found to be entered in duplicate—namely calcitriol (soft gelatinous capsules approved in August 1993 and an injection form approved in March 1994), cepodoxime proxetil tablets (once approved in March 1996 and then approved again in September 1997 under the same category), Saccharomyces boulardii powder (approved in December 1997 but entered twice, once as a yeast preparation and once as a gastrointestinal drug to be used for irritable bowel syndrome), rosiglitazone maleate tablets (approved on 28 June 2000 and then again on 14 July 2000), and growth hormone (approved as genotropin in September 1994 and as somatotropin in February 1998). The repeat entries were removed from the original list, bringing down the total number of entries to 441. In spite of being essentially the same agent, filgrastim (approved as genotropin in September 1994) and G-CSF (approved June 2001) were not treated as duplicate entries in view of the fact that only the later entry was specified as a human recombinant DNA protein.

Of the 441 entries, 28 (6.4%) were veterinary drugs and were excluded from further analysis, as were 17 (3.9%) other drugs whose nature was not understood as they were unfamiliar and not documented in standard textbooks, formularies and reference texts (Table I).3–7 Some products in the latter category appear to be branded compound formulations. This brought the total of further analysable drugs to 396, which was henceforth considered as the denominator for calculation of percentage of total drugs approved.

The entire database entries of approved and analysable agents for human consumption were divided into major categories considering (i) the sheer number of strengths; (ii) biomedical importance with respect to the diseases intended to be treated (e.g. anti-diabetics, antiepileptics, antidepressants, anticancer drugs, etc.); (iii) major pharmacological groups (e.g. quinolone antibacterials, vaccines, analgesics, etc.); and (iv) physiological organ systems at which they were targeted (e.g. ophthalmological agents, dermatological agents, etc.). In most instances, such categorization was already in place, on account of the ATC code assigned to each entry. Where this was not, categories were assigned at the time of analysis. (This database is available from the authors, on request, in Adobe Acrobat portable document format.)

RESULTS

Of the 396 products, 81 (20.5%) were yet to be launched in the Indian market till 31 December 2002. However, some of them, especially the ones approved in the later part of 2002, are likely to be introduced in the near future.

A time-trend curve was constructed for the 15 years, considering the rate of approval of NMEs for each year, along with those 315 products actually introduced. The plot shows an overall rising trend with a sharp escalation in the annual number of product approvals in the new millennium (Fig. 1). The median number of new agents approved annually in this time span was 24 with a mean (SD) of 26.4 (9.52), while the corresponding figures for the agents actually launched were 20 and 21 (5.76), respectively.

Table II gives the major therapeutic categories, and a category-wise listing of approved and launched products.

In addition to therapeutic products, the prophylactic list also underwent expansion with the addition of 11 (2.8%) different vaccines. Three of these are rabies vaccines, including the purified chick embryo cell culture vaccine and inactivated Vero cell vaccine. Others are the oral polio vaccine obtained from the Vero cell line, an injectable vaccine for typhoid fever obtained from the purified Vi capsular polysaccharide of Salmonella typhi, Haemophilus influenzae type B conjugate vaccine, pneumococcal polysaccharide vaccine, an inactivated influenza vaccine, combined DPT–Haemophilus influenzae type B conjugate vaccine, hepatitis A vaccine and the meningococcal type C conjugate vaccine. A parvovirus vaccine was approved but left out of the market.

Two non-vaccine immunobiological products, viz. rabbit antihuman thromocyte globulin and the horse antihuman lymphocyte globulin, have been introduced for immunological rescue in cases of aplastic anaemia.

Subsequent to their introduction, 5 agents were withdrawn from the Indian market. These are the antidepressant amineptine due to its abuse potential, cerivastatin due to alarmingly high rates of rhabdomyolysis reported in some countries, dexfenfluramine on account of valvular heart disease and, recently, astemizole and terfenadine (with effect from 1 April 2003) owing to their propensity to cause QT prolongation and torsades de pointes, and the availability of safer alternatives. Some drugs, such as roxatidine and triflusal, though not withdrawn, have been almost phased out of the market by the manufacturers.

Of the drugs launched in the market and the 315 currently available, at least 61 (19.7%) have spawned related FDCs. Seventy-five (24.2%) are exclusively for parenteral use, 4 drugs are available for use by inhalation (budesonide, fluticasone, ipratropium and salmeterol) apart from the two new inhalation general anaesthetics, while two (nicotine and oestradiol) are available as transdermal delivery systems. Regarding the source, 10 of these 310 (3.2%) are natural products (botulinum neuro-

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Table I. New drug approvals in India during 1988–2002: Products excluded from main analysis

<table>
<thead>
<tr>
<th>Products approved for veterinary use</th>
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<tbody>
<tr>
<td>Amitraz, butafosfane + cyanocobalamin, butalex, cefacetrile sodium, cefotiofur sodium/ceftiofur hydrochloride, clostanel, coligen, cumophos, cypermethrin, danofloxacin mesylate, diazinon, doxazosin, enrofloxacin, equine influenza and rhinopneumonitis vaccine, flavophospholipol flavomycin, flumethrin, maduramicin concentrate, moxidectin, nitroscanate, propanoate + flumethrin, rabies vaccine, salinomycin, semduramycin sodium, sulphachloropyrazine sodium, tiaprost trometamol, toltrazuril, triacendazole, xylazine hydrochloride</td>
</tr>
</tbody>
</table>

Products approved but nature not recognized or possible compound formulations

| BACILLLOCID SPEZIAL*, BRONCHO-VAXOM, centropozine, chelated amino acid based minerals, COMPLEX 15, decapeptide, eerioplast, FORTISON POWDER, PEPTI 2000 LIQUID, KORSOLEX CONCENTRATE, Melagenine, PASPAT, sorbister, SPENGLERSAN, STERILLIUM RUBIN, STRONGER NEO-MINOPHAGEN C, thymogen |

* names of drugs that appeared to be branded compound formulations are given in capitals.
toxin, *Ginkgo biloba* extract, glucomannan, melatonin, nicotine, podophyllotoxin, *Saccharomyces boulardii*, salmon calcitonin [now being synthesized], *Serenoa repens* and silymarin), at least 6 (2%) are recombinant DNA products (alteplase, erythropoietin, G-CSF, growth hormone, insulin lispro, and interferon-a) and 2 (0.7%) are monoclonal antibodies (abciximab and muromonab CD3).

Some products are pure stereoisomers of existing molecules, namely S(-)-amlodipine, esomeprazole, levocetirizine and levofloxacin. The list also includes 9 agents (2.9%) with dependence liability and abuse potential, namely alprazolam, aminepetine (now withdrawn), butorphanol, clobazam, clonazepam, tramadol, zaleplon, zolpidem and zopiclone. Some drugs such as sildenafil and erythropoietin, though without dependence potential, may be misused—the latter by unscrupulous athletes participating in endurance sports. About 96 drugs (31%) are exclusively or predominantly for hospital use.

The number of approvals and introductions of new molecular entities in India, in the major therapeutic categories, during the period of interest have been summed up in Fig. 2.

**DISCUSSION**

The cut-off date for the present analysis was 31 December 2002. This implies that some of the products approved after that date but not available as yet may still be introduced in the future. It is also possible that a product not approved in India but duly approved in other countries may be imported in reasonable quantity on a named patient basis. This is permitted by the Government of India (vide notification available on Central Drugs Standard Control Organization website at http://cdsco.nic.in).

The annual rate of approval of new drugs in India is comparable with the US FDA data over the past 5 years (median, 24 v. 27; mean [SD] 26.4 [9.52] v. 26.6 [6.73]). The European Medicines Evaluation Agency (EMEA) of the European Union approved 24 new drug applications in 2002. Thus, the rate in India appears to be at par with developed markets. However, there has been a substantial spurt in the past 2 years. Possibly, this is propelled by India’s impending accession to the product patent regime in accordance with the directives of the World Trade Organization–Trade Related Aspect of Intellectual Property Rights (WTO–TRIPS) agreement. Indian companies probably want to bring in as many new molecules into the market as possible before the WTO–TRIPS cut-off date of January 2005. The situation thereafter may not allow introduction of patented molecules so readily.

The time lag between Indian and US FDA approval has been about 2 years (ranging from 3 months to 4 years), the Indian approval usually being the one to follow. This has been a little less for anticancer drugs (average lag of 1.6 years, range 5 months to 2.5 years). However, there are also instances such as ketotifen (8.16 years), pantoprazole (1.16 years), meloxicam (1.16 years), rivastigmine (1.75 years), triptorelin acetate (6.91 years), ritonavir (3 years), desloratidine (0.16 years), and oxaliplatin (3.83 years) where the Indian approval dates actually preceded their American counterparts.

**Omissions from the list**

Our list does not include some NMEs that have become available in India within the past 15 years. Thus, enoxaparin sodium is the only low molecular weight heparin listed, although ardeparin, certoparin, dalteparin, gensparin, nadoparin, parnaparin, reviparin and tinzaparin are also available. Other omissions include coenzyme Q10, the adjuvant anti-anginal trimetazidine, the nootropic piracetam, the anti-asthmatic formoterol, the oral iron chelator deferiprone, the parenteral antihypertensive enalaprilat, fentanyl transdermal patch for intractable pain, the granulocyte–monocyte colony stimulating factor molgramostim, human diploid cell rabies vaccine, attenuated varicella vaccine, and the radiocontrast medium ioxithalam. We were unable to ascertain whether these are genuine omissions from the lists made public or whether the lists we received were incomplete. It is also plausible that products may be available in India under an import licence only, in which case they may not get reflected in the new drug approvals list.

Some single-ingredient plant products have been included in our analysis but there are also omissions such as extracts of *Hypericum perforatum* (St John’s wort) as antidepressant, *Tinospora cordifolia* as immunomodulator and *Phyllanthus amarus* as a hepatoprotective agent in viral hepatitis. Possibly,
Cardiovascular drugs

• Pediculicide and scabicide: permethrin
  Ectoparasiticides (launched 1, 0.25%)
  • trapidil* (adjunct in angioplasty)
  • creatine phosphate
  • calcium dobesilate (vasoactive agent)
  • amrinone, dobutamine and milrinone (inotropic agents)
  • adenosine, amiodarone and flecainide* (antiarrhythmics)
  Others (launched 9, 2.27%)
  • eptifibatide, clopidogrel, ticlopidine and triflusal (other antiplatelet drugs)
  • enoxaparin (a low molecular weight heparin)
  • alteplase (human recombinant tissue plasminogen activator or r-tPA)
  • abciximab (antiplatelet monoclonal antibody)
  Fibrates: bezafibrate, fenofibrate, gemfibrozil
  Statins: atorvastatin, cerivastatin, lovastatin, pravastatin and simvastatin

Hypolipidaemic drugs (launched 8, 2.02%)

Antihypertensives, antianginals and anti-heart failure drugs (launched 27, 6.82%)

• 1-adrenergic receptor blockers: doxazosin, prazosin and terazosin
  Antileishmanial agents||: miltefosine*
  • Nitroimidazoles: tinidazole and secnidazole
  • Antimalarials: artemether, artesunate, arte-ether, mefloquine and bulaquine

Others (launched 13, 3.28%)

Central nervous system and allied drugs

Antidepressants (launched 11, 2.78%)

• amineptine, bupropion, citalopram, clomipramine, fluoxetine, fluvoxamine,
  lofepramine*, mirtazapine, moclobemide, paroxetine, reboxetine*, sertraline, venlafaxine
Antipsychotics (launched 8, 2.02%)

• clozapine, haloperidol, loxapine, olanzapine, perphenazine, quetiapine,
  risperdone, sulpiride*, ziprasidone*, zuclopenthixol
Antiepileptics (launched 7, 1.77%)

• clobazam, clonazepam, divalproex sodium, gabapentin, lamotrigine,
  oxcarbazepine, phenytoin sodium*, topiramate
Anti-parkinsonian agents (launched 3, 0.76%)

• cabergoline*, piribedil, ropinirole, selegiline

Drugs to combat addictive disorders (launched 4, 1.01%)

• acamprosate calcium* (anticraving drug to prevent relapse in detoxified
  alcoholics)
• bupropion (in addition to its role as antidepressant) and nicotine (in
  transdermal patch formulation) to facilitate smoking cessation
• naltrexone and nalmefene (opioid antagonists)

Analgesics (launched 14, 3.54%)

• benzydamine (NSAID-like topical agent), butorphenol (opioid), celecoxib,
  etodolac*, felbina*, ketorolac, meloxicam, nabumetone, nifopam,
  nimesulide, parecoxib, rofecoxib, tenoxicam, tolfenamic acid, tramadol
  (opioid-like) and valdecoxib

General anaesthetics (launched 4, 1.01%)

• isoflurane and sevoflurane (inhaled)
• midazolam and propofol (parenteral)

Skeletal muscle relaxants (launched 5, 1.26%)

• baclofen and tizanidine (centrally acting)
• botulinum neurotoxin
• metaxalone*, pipecuronium and rocuronium (peripheral neuromuscular
  blockers)
• thiocholchicoside*

Others (launched 10, 2.53%)

• alprazolam, buspirone (anxiolytics)
• donepezil, rivastigmine, tacrine* (for dementias such as Alzheimer disease)
• flunarizine (for mitigating migraine headache)
• Gingko biloba extract
• idebenone*
• ilidizole* (for motor neuron disease)
• sumatriptan (for controlling acute migraine attacks)
• tetrabenazine (for involuntary movement disorders)
• vinpocetine*
• zolpidem, zopiclone, zaleplon* (sedative–hypnotics)

Gastrointestinal drugs

Drugs for acid peptic disorders (launched 9, 2.27%)

• Colloidal bismuth preparation: tripotassium dicitrato bismuthate
• H2-receptor blockers: famotidine and ranitidine
• Proton pump inhibitors: esomeprazole, lansoprazole, omeprazole, pantoprazole
  and rabeprazole
• Prostacyclin analogue: misoprostol

Others (launched 13, 3.28%)

• 5-amino salicylic acid (for ulcerative colitis)
• balsalazide* (aminosalicylate for ulcerative colitis)
• cisapride, itopride and mosapride (prokinetic agents)
• dexfenfluramine and sibutramine (antiobesity agents)
• grani slighton and ondansetron (antiserotonergic antiemetics)

(contd.)
Considering antimicrobials as a broad class, encompassing antibacterials, antivirals, antifungals, as well as antiprotozoals and anthelmintrics, a total of 61 agents (15.4%) were approved but were yet to be introduced by 31 December 2002.

Cephalosporins and quinolones taken together account for about two-thirds of all the antibacterials launched. None of the 15 cephalosporins and 9 quinolones approved were left to be introduced.

Many of these agents have already been listed in earlier categories. Dermatological line extensions of existing molecules have been excluded from the analysis.

Although approved, the antitussive prenodoxazone and the pulmonary surfactants colfosceril palmitate and poractant alfa are yet to be generally available.

No new diuretics were approved or introduced during the study period.

Miltefosine was approved in March 2002, but is still to be launched, presumably because of the substantial toxicity and the potential for rapid emergence of resistance.

Antiretrovirals have all been introduced within the past five years except zidovudine that was approved in 1988.

Antithrombins: (launch, 2003).

No new chemotherapeutic and immunotherapeutic agents were approved or introduced during the study period.

No new corticosteroids were approved or introduced during the study period.

No new antidiabetics were approved or introduced during the study period.

No new endocrine therapy for cancer agents were approved or introduced during the study period.

No new radiological contrast media agents were approved or introduced during the study period.

No new miscellaneous drugs were approved or introduced during the study period.

**Table II. Selective listing of new drugs in India during 1988–2002 (contd.)**

<table>
<thead>
<tr>
<th>Category</th>
<th>Launch Period</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapeutic and immunotherapeutic agents</td>
<td>1988–2002</td>
<td>3.54%</td>
</tr>
<tr>
<td>Anticancer drugs, anticancer adjuvants and immunomodulating agents</td>
<td>1988–2002</td>
<td>3.54%</td>
</tr>
<tr>
<td>Endocrine therapy for cancer</td>
<td>1988–2002</td>
<td>3.54%</td>
</tr>
<tr>
<td>For supportive role in cancer chemotherapy</td>
<td>1988–2002</td>
<td>3.54%</td>
</tr>
</tbody>
</table>

* approved but were yet to be introduced by 31 December 2002.
††† Antiretrovirals have all been introduced within the past five years except zidovudine that was approved in 1988.
‡‡‡ Although approved, the antitussive prenodoxazone and the pulmonary surfactants colfosceril palmitate and poractant alfa are yet to be generally available.
†‡‡ Many of these agents have already been listed in earlier categories. Dermatological line extensions of existing molecules have been excluded from the analysis.
some of these agents are being marketed under Ayurvedic licence and so would not be included in our list. The case may be similar with agents that are marketed as food supplements or ‘proprietary foods’ rather than under a drug licence, such as alpha-lipoic acid, aspartame, chromium picolinate, glucosamine-chondroitin, and the n3-polyunsaturated fatty acids eicosapentaenoic acid and docosahexaenoic acid.

Reasons for the rapid and huge proliferation

In today’s world, a pharmaceutical company is profit-oriented and answerable to its shareholders rather than to prescribers or patients. Market dynamics dictate that drugs which need to be continued lifelong provide a more lucrative business proposition than those that are used for a short duration, occasionally or in uncommon disorders. Consequently, molecules such as first-line antihypertensives (dihydropyridine calcium-channel blockers, ACE inhibitors, angiotensin II receptor blockers), antiplatelet-antithrombotics, lipid-lowering agents especially statins, antidiabetic agents, and so on, are treated as real money-spiners and are launched and promoted by companies with great fanfare and zeal. The same holds good for drugs that are not necessarily for lifelong use but are likely to be used frequently or for considerable lengths of time, such as proton pump inhibitors, antidepressants, antiasthmatics and non-sedating anti-allergics. Predictably, once approved delay seldom occurs in launching such a molecule. The same vigour is adopted for short-use, expensive products. Thus the promotion is disproportionately high for molecules such as cephalosporins, quinolones, new parenteral antibiotics and novel antithrombotics for acute coronary and cerebrovascular events. The possible surprising exception is enoxaparin, approved way back in 1992 but introduced much later.

Multiple ploys are adopted by the companies to expand and retain their market share at the cost of rational therapeutics. When patents are on the verge of lapsing or new entrants threaten the market share, range extensions such as modified release preparations, new salts or esters, and new dosage forms appear in the market. An interesting recent trend is the introduction of pure stereoisomers (examples have been mentioned earlier), few of which offer substantial advantages over the racemates available for so long. This trend is likely to continue with escitalopram and S (–)-salbutamol waiting in the wings.

Practitioners’ attitudes may also encourage the proliferation of new drugs. The fascination with a particular product, whether justified by scientific evidence or not, leads to proliferation of brands and introduction of close congeners. Whether this is the cause or result of aggressive marketing by the companies, is difficult to ascertain; but the result is that more and more doctors tend to prescribe these products, without a balanced judgement of their risks and benefits in a given situation. Though a relatively new group of molecules among analgesics, the selective COX-2 inhibitors are already showing this disturbing trend. Experience suggests that some new entrants, introduced too precipitously (cerivastatin) may actually do more harm than good.

The unrestrained brand proliferation that follows the introduction of a new molecule in India is a phenomenon without parallel elsewhere in the world. For instance clopidogrel, approved in February 2001, spawned at least 16 brands within a year of approval; gatifloxacin, approved in October 2001, has at least 20 brands till date; while valdecoxib, cleared only in August 2002, has at least 10 brands already. Companies, in their eagerness to snatch whatever share of the market they can, come to strange marketing arrangements. Thus, there is promotion of the same brand by two different companies, promotion of the same product by two different divisions of the same company, simultaneous promotion of closely related congeners that confuse the prescribers, not to mention the various unethical inducements offered to some practitioners, retailers and other players in the drug trade. Perhaps the only silver lining is that competition may force lowering of prices. Such dramatic price cuts, sometimes to even less than one-third the introductory price within months, have been seen with atorvastatin, clopidogrel, gatifloxacin, etc. That brand proliferation could lead to such rapid and remarkable price decline suggests that the initial high pricing was arbitrary, rather than linked to genuine research or production costs, and had been fixed only with the aim of maximizing profit.

Major therapeutic advances are rare

Despite such rapid proliferation of new molecules it remains an acknowledged fact that real therapeutic advances are rare.9 Each year, only a handful of the molecules introduced globally represent breakthroughs or tangible advances in therapeutic problem areas. It is also estimated that less than 10% of medical research spending worldwide is allocated to diseases affecting 90% of the world’s population, i.e. people living in poor countries.10 For example, the two biggest killers, diarrhoea and pneumonia in children, account for 11% of the mortality worldwide, but receive only 0.2% of the available research funding. In our list too, few molecules can be said to relate to specific infectious disease problems in India. Malaria is the only exception. The activity in other segments tends to reduce attention and research funds from therapeutically starved areas. Curiously enough, major advances in ‘un glamorous’ areas may go unnoticed if the products do not offer the prospect of substantial profit to the companies. Folic acid in neural tube defects and ivermectin in scabies are two examples.

Policy shortcomings and lapses

In most strictly regulated pharmaceutical markets, new FDCs are treated as new drugs and so have to clear the same stringent quality and clinical trial norms. Unfortunately, although they are meant to be considered as new drugs in India too, their licensing by various state drug control authorities is liberal. This has led to a plethora of FDCs in the Indian market today (our analysis shows that one-fifth of the currently available new drugs are available as FDCs), with few having a definite rationale other than patient compliance. For instance, there are FDCs of metformin with all the other oral hypoglycaemic drugs except repaglinide and nateglinide. The pharmacokinetic and clinical trial data submitted by manufacturers in support of their FDCs, if at all, are not accessible to doctors or the public.

Indeed, though this is the information age, it is difficult to get impartial information on new drugs in India. We had to expend considerable energy just to acquire the list of approved drugs. There are no systematic efforts to update prescribers regarding new drugs and their place in therapeutics. Admittedly, practitioners must share the blame for failing to delve into the medical literature, apart from those disseminated selectively by medical representatives, but it is also a fact that they are often too overburdened to spare time for continuing medical education. However, as drugs proliferate, this unmet information need will also continue to grow. Therefore, there is an urgent need to evolve a system whereby all practitioners get the time and opportunity to upgrade their professional knowledge. Professional bodies of doctors can make the effort to build up public opinion and create
pressure so as to make the legislature take note and pass laws such as those by the European Parliament in October 2002, aimed at guaranteeing access to drug information for all European citizens. This would also ensure at least some safeguarding of public interest in the WTO–TRIPS era.

New drugs also mean new adverse drug reactions. Unfortunately, at this juncture, we lack a nationwide pharmacovigilance system. There are isolated efforts, based at a few tertiary centres and supported by the Indian Council of Medical Research, to monitor adverse drug reactions. The recent efforts by the Central Drugs Standard Control Organization to set up a countrywide network is laudable and needs to be encouraged. Without such a system, we will never have the indigenous data to properly judge the risk–benefit profiles of new drugs in India.

**Implications for medical education**

The rapid pace of proliferation of new drugs, without corresponding access to impartial information, tends to leave trainee doctors confused but tempted to prescribe new remedies without adequate knowledge. It is here that conscientious medical teachers and clinicians, who take the trouble to genuinely update themselves about new drugs, can serve as appropriate role models for tomorrow’s doctors. The basic medical curriculum should stress on the core principles in pharmacology and therapeutics which would equip the students to themselves make a rational choice from among the plethora of alternatives, rather than on cramming information. Core knowledge and the ability to make an informed choice has to be the goal of basic pharmacology and therapeutics education today.

The pharmaceutical field is highly dynamic. A drug that is essential today may be obsolete tomorrow or one that is inconspicuous now may become indispensable in future. Between such extremes, there will always be numerous molecules whose therapeutic utility would need constant reappraisal. New diseases keep on emerging. New drugs proliferate even more rapidly. Therefore, knowledge of the trends in new drug introductions is essential to keep therapeutic gains in perspective amid this confusion.

**REFERENCES**