The delay of castor oil-induced diarrhea has been demonstrated to characterize non-steroidal anti-inflammatory drugs (NSAIDs). Awounters et al. tested 44 NSAIDs and found that the selective potencies of the drugs in castor oil-induced diarrhea and in the carrageenin-induced test correlated well. The sodium curcuminate was found to be more effective in inhibiting carrageenin-induced rat paw edema when compared with curcumin and some of its semisynthetic analogues.

The delay of castor oil-induced diarrhea and the inhibition of carrageenin-induced inflammation by sodium curcuminate may be related to the inhibition of prostaglandin synthesis.

In earlier studies, sodium curcuminate has been shown to antagonize the contractions of isolated guinea pig ileum induced by various agonists. This property is also shared by most of the NSAIDs. The inherent resting tone of the intestinal smooth muscle is known to be maintained by continuous intramural generation of prostaglandins and the inhibition of prostaglandin biosynthesis by NSAIDs results in decrease of the resting tone. Sodium curcuminate has been shown to produce a similar decrease in the resting tone of rabbit intestine.

Hence, it may be quite possible that all these activities could be attributed, at least partly, to inhibition of prostaglandin biosynthesis. However, further studies are required to understand the mechanism that might account for the antiinflammatory and related action of sodium curcuminate.

**Table 1**

<table>
<thead>
<tr>
<th>Drug per kg, b.w. at 0 h*+ castor oil 1 ml, p.o., at 1 h</th>
<th>Mean number of wet faeces</th>
<th>% Inhibition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (Water, 5 ml)</td>
<td>6.66 ± 0.71</td>
<td>–</td>
</tr>
<tr>
<td>Indomethacin (10 mg)</td>
<td>0.66 ± 0.33†</td>
<td>90.09</td>
</tr>
<tr>
<td>Sodium curcuminate (0.1 mg)</td>
<td>4.16 ± 0.47†</td>
<td>37.53</td>
</tr>
<tr>
<td>Sodium curcuminate (0.2 mg)</td>
<td>3.50 ± 0.49†</td>
<td>47.45</td>
</tr>
<tr>
<td>Sodium curcuminate (0.6 mg)</td>
<td>2.16 ± 0.60†</td>
<td>67.56</td>
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<tr>
<td>Sodium curcuminate (1 mg)</td>
<td>1.33 ± 0.55†</td>
<td>80.03</td>
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</table>

*The test drug and vehicle were given p.o. and indomethacin was given i.p., values are mean±SEM, n = 6 in each group. † P < 0.001 when compared to control

**References**


**Therapeutic substitution: A hidden irrationality**

Sir,

It cannot be denied that irrationality is widely prevalent in the field of medicine. Doctors with wrong practices, pharmaceutical companies with their promotional tactics, patients indulging in self-medication and the government’s inability in implementing an effective and efficient drug control system are some of the known apparent factors responsible for irrational drug therapy. But one of the serious factors on the part of the pharmacist is drug substitution, which still remains hidden and can contribute significantly to the irrationality. When a prescription is written for a proprietary product, the pharmacists must, under the law, dispense that product only, unless they persuade the doctor to alter the prescription. Under such circumstances they can substitute a generic product for the proprietary formulation prescribed by the doctor (Generic Substitution). But indulging in therapeutic substitution is a serious irrationality on the part of the pharmacists where a drug belonging to same class but with a different chemical structure is deemed to be pharmacologically and therapeutically equivalent and is used as a substitute. This can cause serious adverse therapeutic outcomes and therapeutic failures. This also denies the doctors’ right to prescribe their priority drug for a given indication as well as denies the patients’ right to have chemically same drug prescribed by a doctor. Therefore, it also has legal implications.

Drug substitution is done quite often by the pharmacist and studies had not been carried out on this aspect in the past. Therefore, a prospective study was carried out by collecting 200 prescriptions from patients/relatives who, after attending the OPDs of different departments, had visited different chemist shops near the Government Medical College, Jammu to purchase prescribed drugs. The prescribed drugs in the prescriptions were compared with the actual drugs received by the patients/relatives from the chemist shops for evaluating the total drug substitutions, generic substitutions and therapeutic substitutions in the prescriptions. The incidence of each group of drugs in prescriptions showing generic substitution and therapeutic substitution was also worked out. The present study was irrespective of the total number of drugs substituted in one prescription and the number of visits of patients/relatives. An interview or questionnaire study of the patients/relatives and chemists to ascertain the cause of drug substitution was not done as diverse answers and reactions were expected. Moreover, lack of cooperation on the part of the chemists interfering with the outcome of study was feared. Doctor-patient interactions were also not studied; the present study concentrated only on therapeutic transactions.

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**Research Letter**

**Table 1**

**Effect of sodium curcuminate on castor oil-induced diarrhea in rats**

<table>
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<tr>
<th>Drug per kg, b.w. at 0 h*+ castor oil 1 ml, p.o., at 1 h</th>
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*The test drug and vehicle were given p.o. and indomethacin was given i.p., values are mean±SEM, n = 6 in each group. † P < 0.001 when compared to control
Drugs (10.25%) and (27.77%) respectively. Drug substitution ease (20.5%) and (16.66%), and analgesic/antiinflammatory (46.15%) and (44.44%), followed by drugs for peptic ulcer disease (20.5%) and (16.66%), and analgesic/antiinflammatory drugs (10.25%) and (27.77%) respectively. Drug substitution was also seen with preparations like vitamins, minerals and hematinics, antihistaminics, antianxiety drugs, antihypertensives and cough syrups as shown in Table 1. The patients/relatives were very cooperative but there were mixed reactions from the chemists while conducting the study. The present study indicated drug substitution to be quite prevalent in the society. Using non-proprietary names to prescribe drugs can be cost-effective to the patients and can also tackle the problem of the “Therapeutic Jungle”.5 We suggest that therapeutic substitution could also be curtailed by writing non-proprietary name of the drugs in prescriptions.

In conclusion, the drug control system of the government must recognize this serious hidden irrationality on the part of the pharmacist in the overall interest of the society.

The results are shown in Table 1. In the present study 28.5% of the total prescriptions showed drug substitution. Out of these prescriptions 19.5% were found to be substituted generically whereas 9% of these prescriptions showed therapeutic substitution. The incidence of each group of drugs in prescriptions showing generic substitution and therapeutic substitution was observed. It was the maximum with antibiotics (46.15%) and (44.44%), followed by drugs for peptic ulcer disease (20.5%) and (16.66%), and analgesic/antiinflammatory drugs (10.25%) and (27.77%) respectively. Drug substitution was also seen with preparations like vitamins, minerals and hematinics, antihistaminics, antianxiety drugs, antihypertensives and cough syrups as shown in Table 1. The patients/relatives were very cooperative but there were mixed reactions from the chemists while conducting the study. The present study indicated drug substitution to be quite prevalent in the society. Using non-proprietary names to prescribe drugs can be cost-effective to the patients and can also tackle the problem of the “Therapeutic Jungle”. We suggest that therapeutic substitution could also be curtailed by writing non-proprietary name of the drugs in prescriptions.

In conclusion, the drug control system of the government must recognize this serious hidden irrationality on the part of the pharmacist in the overall interest of the society.

Table 1: Drug substitution

<table>
<thead>
<tr>
<th>Prescriptions evaluated</th>
<th>200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescriptions showing drug substitution</td>
<td>57 (28.5)</td>
</tr>
<tr>
<td>Prescriptions showing generic substitution</td>
<td>39 (19.5)</td>
</tr>
<tr>
<td>Prescriptions showing therapeutic substitution</td>
<td>18 (9)</td>
</tr>
</tbody>
</table>

Incidence of each group of drugs in prescriptions showing generic substitution:

- Antibiotics: 18 (46.15)
- Peptic ulcer disease: 8 (20.50)
- Analgesic/antiinflammatory: 4 (10.25)
- Vitamins, minerals and hematinics: 4 (10.25)
- Antihistaminics: 2 (5.12)
- Antianxiety drugs: 2 (5.12)
- Antihypertensive drugs: 1 (2.56)

Incidence of each group of drugs in prescriptions showing therapeutic substitution:

Prescribed | Substituted
---|---
Antibiotics 8 (44.44) | Cefadroxil | Cefaclor
| Metronidazole | Tinidazole
| Amoxicillin | Ampicillin
| Amoxicillin+Clavulanic Acid | Ampicillin+Clavulanic Acid
| Norfloxacin | Ofloxacain
| Gatifloxacin | Ciprofloxacin
| Norfloxacin+Tinidazole | Ciprofloxacin+Tinidazole
| Cefotaxime* | Ceftriaxone

Analgesic/antiinflammatory drugs 5 (27.77)

Nimesulide | Paracetamol
| Nimesulide+Paracetamol
| Diclofenac Na | Ibuprofen
| Diclofenac Na* | Diclofenac Na*
| Valdecoxib | Celecoxib

Peptic ulcer disease drugs 3 (16.16)

Ranitidine | Famotidine
| Omeprazole | Lansoprazole
| Prolinat (Omeprazole + Metronidazole) | Omeprazole + Metronidazole+Amoxicillin
| Cough syrup 1 (5.55) | Salbutamol+Guaifenesin
| Pseudoephedrine | (Dextromethorphan+Tripolidine)
| Antihypertensive drugs 1 (5.55) | Losartan + Enalapril

* Represents parenteral preparation. Figures represent n (%)