Therapeutic Review

Tartrazine: a potentially hazardous dye in Canadian drugs

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The literature was reviewed to determine the incidence of idiosyncratic reactions to tartrazine. From 4% to 14% of individuals with asthma or allergies or both and from 7% to 20% of persons who are sensitive to acetylsalicylic acid may react to this dye. The mechanism of such reactions is unknown. Pharmaceutical manufacturers and distributors were surveyed and a list was prepared of approximately 450 Canadian pharmaceuticals that contain tartrazine. The 53 pharmaceutical manufacturers and distributors whose drug products do not contain this dye were also listed. It is recommended that information concerning the tartrazine content of drugs be included on package labels.

On a fait une revue de la littérature afin de déterminer la fréquence des réactions idiosyncrasiques à la tartrazine. De 4% à 14% des individus souffrant d'asthme ou d'allergie, ou les deux, et de 7% à 20% des personnes sensibles à l'acide acétylsalicylique peuvent réagir à ce colorant. Le mécanisme de ces réactions est inconnu. Une enquête a été menée chez les fabricants et distributeurs de produits pharmaceutiques à partir de laquelle on a dressé une liste d'environ 450 préparations pharmaceutiques canadiennes contenant de la tartrazine. On a également fait une liste de 53 fabricants ou distributeurs de produits pharmaceutiques dont les médicaments ne contiennent pas de tartrazine. On recommande que de l'information relative à la teneur en tartrazine des médicaments fasse partie de l'étiquette apposée sur le contenant.

Dyes are an important ingredient in the processing of foods and in the manufacture of drugs and cosmetics. They are widely used, and consumers tend to expect and accept their presence. Yet several dyes, particularly those derived from coal tar and those that have an aniline or azo structure, have been reported to cause allergic reactions.[1-5] Dyes such as tartrazine, amaranth, sunset yellow, FD&C (Food, Drug and Cosmetic [Act] — USA) no. 6 and new coccine have all been implicated in hypersensitivity reactions.[1-5] However, the association of such reactions with tartrazine has received the most publicity.

Tartrazine (FD&C no. 5, Colour Index [CI] food yellow 4) is a monazo dye derived from coal tar.[6] It exists as a bright yellow–orange powder that is freely soluble in water. It becomes redder in the presence of sodium hydroxide,[7] and if it is mixed with blue a lime-green colour results. At least 60 countries have approved this dye, and it is one of the nine colours permitted for use in food in Canada.[6]

Many processed foods contain the dye, including some dairy products, juices, pickles, candies and cake mixes, as do most home food-colouring kits.[6] Cosmetics and toiletries, such as shampoos, after-shave lotions, colognes, toothpastes and soaps, may all contain tartrazine. Pharmaceutical manufacturers use this dye in many types of drug products. Tablets and capsules may contain tartrazine in coatings, shells and excipient materials.[8] Other dosage forms in which tartrazine may be found include liquids for ingestion, lozenges, ointments and douches. The amount of tartrazine found per dosage unit is usually very small — probably within the range of 0.001 to 2.5 mg (written communication from Canadian pharmaceutical manufacturers, 1981). Idiosyncratic reactions have been reported to occur following the ingestion of drug products containing such small amounts.[2,4] As well, a tartrazine-containing enema was reported to have caused an anaphylactoid reaction.[5] There have been no reports in the literature of allergic reactions occurring because of the topical application of drug products containing tartrazine.

Several family physicians in active practice had commented to me that they have not encountered a patient in whom they had recognized a sensitivity to tartrazine. Partly in response to these comments I reviewed the literature to determine the incidence and mechanism of reactions to this dye and the characteristics of patients at greatest risk of such reactions.

Canadian pharmaceutical manufacturers are not required to indicate the dye content of their drug products on the package labels. Manufacturers were surveyed for this information, and from data they supplied two lists were compiled. One is a list of the pharmaceutical manufacturers and distributors whose Canadian products do not contain tartrazine (Table I). The other is a list of drug products manufactured or distributed, or both, in Canada that contain tartrazine and are intended for oral use (Table II).

Literature review

Idiosyncratic reactions to tartrazine

The first report of a reaction secondary to the ingestion of medication containing tartrazine appeared in 1959. Lockey[2] reported on three patients who reacted to tartrazine present in three different corticosteroid products. Since then more than 25 cases of tartrazine sensitivity have been reported.[9] The reactions, which occur most commonly in patients with acetylsalicylic acid (ASA) sensitivity, may vary from mild to severe. Patients with this sensitivity have been described as presenting with the following: severe pruritus with generalized

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urticaria,[2,4,5,10,11] edema of the lips, tongue or uvula,[2,4] wheezing and asthmatic attacks,[4,10,12] periorbital swelling,[2,10] blurred vision,[4,11] conjunctival irritation,[10] increased nasopharyngeal secretions,[11] a feeling of warmth and suffocation,[11] palpitations,[11] anaphylaxis,[5,12] severe headache,[2] vomiting,[2] and tingling of the mouth and tongue.[2,4] There have been three reports of a reaction occurring in a patient not sensitive to ASA.[5,13,14] Two of these patients presented with systemic anaphylaxis.[5,13]

The prevalence of tartrazine sensitivity is not known, but it has been suggested to be 1 in 10 000.[8] Several researchers have attempted to predict the incidence of tartrazine sensitivity in asthmatic or allergic individuals. Settipane and associates[15] conducted a double-blind, crossover challenge test using 0.22 mg of tartrazine and placebo in a group of patients with at least a 2-month history of chronic urticaria. Of the 22 patients tested, 3 (14%) had an exacerbation of urticaria within 3 hours of the tartrazine challenge. Farr and colleagues[16] reported that 11 (4%) of 277 asthmatic individuals challenged with 1 to 50 mg of tartrazine had a 20% or greater reduction in forced expiratory volume within 4 hours of ingestion.

In a single-blind study of 122 patients (97 with allergic disorders, 25 without), 32 (26%) had an allergic reaction to 50 mg of tartrazine within 15 minutes;[11] the 32 who reacted were all described as having "allergic disorders", whereas none of the "nonallergic" patients reacted. Although the dose of tartrazine used in this study was several times greater than the amount of tartrazine usually found in medications, a lower dose (10 mg) produced the same response in the four patients who were rechallenged.

From these reports it appears that the incidence of tartrazine idiosyncratic reactions in allergic and asthmatic individuals ranges from 4% to 14% and may be as high as 26%.

Cross-reactivity with ASA

A cross-reaction between ASA and tartrazine was first reported in 1967 by Samter and Beers.[17] In their double-blind study, which was reported in summary form only, cross-reactivity occurred in 7.5% of patients known to be allergic to ASA who were given a 25-mg dose of tartrazine. Delaney,[18] in a single-blind study in which 35 patients with a history of asthma and ASA idiosyncratic reactions were given 25 mg of tartrazine and placebo, observed cross-reactivity in a similar percentage (7%). Settipane and associates[15] reported a double-blind study in which they administered 0.22 mg of tartrazine and placebo to 10 patients with ASA intolerance; 2 (20%) reacted to the tartrazine.

In a carefully designed project Settipane and Pudupakkam[19] used a double-blind crossover method to study known ASA reactors and matched nonreactors. All subjects were challenged with 0.22 or 0.44 mg of tartrazine and placebo. Of the 40 ASA reactors 6 (15%) reacted adversely to tartrazine but not to the placebo. The subjects reacted to tartrazine in the way that they did to ASA; that is, those who reacted to ASA with generalized itch and urticaria had similar symptoms after taking tartrazine, while those in whom ASA caused bronchospasm had a similar reaction to tartrazine. None of the controls reacted to tartrazine.

These studies indicate that the incidence of cross-reactivity to ASA and tartrazine ranges from 7% to 20%.

In contrast, Speer and coworkers[20] recently reported on a 17-year prospective study of the clinical characteristics of patients with a history of allergic reactions to ASA. Only 4 (2%) of their 205 ASA-allergic patients also reacted to tartrazine. Therefore, they were unable to confirm that tartrazine cross-reacts with ASA.

Mechanism of idiosyncratic reactions to tartrazine

The mechanism of idiosyncratic reactions to tartrazine is not known. Because of possible cross-reactivity between ASA and tartrazine it has been suggested that these substances cause reactions by the same mechanism. Recent suspicion that idiosyncratic reactions to ASA may be due to inhibition of prostaglandins from series E[21] has led to research on whether tartrazine also interferes with prostaglandins, but no such effect has been observed.[22,23]

Studies of the role of immunoglobulins in ASA and tartrazine intolerance have shown that IgA, IgE and IgM do not mediate the idiosyncratic reactions.[11,24] However, one investigator has reported a correlation between IgD levels in the serum and tartrazine hypersensitivity.[25]

The metabolite of tartrazine, sulfanilic acid, was found not to produce idiosyncratic reactions.[3] Neuman and colleagues[11] suggested that an excess of vasoactive material, such as bradykinin, may be associated with the reaction. Nevertheless, the actual mechanism of the tartrazine hypersensitivity reaction remains unknown.

Table I—Pharmaceutical manufacturers and distributors whose Canadian drug products do not contain tartrazine

Adrem Limited	Halocarbon (Ontario) Ltd.	Pharmacia (Canada) Ltd/Ltée
Alcon Laboratories Ltd.	ICI Pharmaceuticals	Robinson & Webber (1978) Ltd.
Allergan Inc.	Johnson & Johnson Inc.	Roussel (Canada) Inc.‡
Alza Pharmaceuticals	K-Line Pharmaceuticals Ltd.	Schering Canada Inc.*
Austin Laboratories (Canada) Ltd.	Kremers-Urban (Canada)	Julius Schmid of Canada Limited
Ayerst Laboratories	Lewis-Howe Company*	Scholl (Canada) Inc.
Baxter Travenol Laboratories of Canada Ltd.	Eli Lilly & Company (Canada) Limited†	Shaklee Canada Inc.
Brioschi Inc.	Mallinckrodt Canada Inc.	Smith & Nephew Inc.
Burton, Parsons	Maltby Brothers Limited	Syntex Inc.
Carter Products	Marion Laboratories Inc.	Texcan Pharmaceuticals Limited
A.W. Chase	Jeffrey Martin, Inc.	Therapex-Unik Inc.
Commerce Drug (Canada), Inc.	Medinex Limited/Limitée	Trans Canada Contact Lens Ltd.
Cress Laboratories Ltd.	The T. Milburn Company Ltd.	Trans-Canada Dermapeutics Ltd.
Cutter Ltd.	Novopharm Limited	Unimed Canada Incorporated
Daillac Limitée	Odan Laboratories Ltd.	Wampole Inc.*
Dispar Veterinary Products Ltd.	Owen Laboratories	Westwood Pharmaceuticals
Elliott-Marion	Person & Covey, Inc.	Whitehall Laboratories Limited
Ex-Lax Ltd.	Pfizer Canada Inc.	

*Products recently reformulated without tartrazine.
†See individual Lilly products in Table II.
‡Tartrazine recently removed from Rythmodan 100-mg capsules.

Table II—Drug products manufactured or distributed in Canada, or both, that contain tartrazine

ABS & C tablets-Cert. (Drug Trading)
ABS & C tablets IDA (Drug Trading)
Achrocidin tabs (Lederle) (2nd, 1984)*†
Achromycin V caps 250 mg (Lederle) (3rd, 1986)*†
Actifed-Plus Syrup (BW Inc.)
Actifed Syrup (BW Inc.)
Adenex tabs (ICN)
Adroyd tabs 5 mg (Parke-Davis)
Aldactazide tabs (Searle)
Aldactone tabs 25 & 100 mg (Searle)
Aldomet tabs 125, 250 & 500 mg (MSD)
Alka Butazolidin tabs (Ciba)
Alka Tandearil tabs (Geigy)
Alkabutazone tabs (ICN)
Amitriptyline tabs 25 & 50 mg (Sands)
Amoxican caps 250 & 500 mg (ICN)
Amoxican susp. 250 mg (ICN)
Ampicillin caps 250 & 500 mg (Sands)
Ampicin caps 250 & 500 mg (Bristol)
Amytal tabs 30 mg (Lilly)‡§
Anadol-C½ tabs (Dow)
Anafranil tabs 10 & 25 mg (Geigy)
Anthrombin-K tabs 2 mg (Purdue Frederick)
Apo-imipramine tabs 10, 25 & 50 mg (Apotex)
Apo-methyldopa tabs 125, 250 & 500 mg (Apotex)
Apo-thioridazine tabs 25 mg (Apotex)
Apresoline 10 mg (Ciba)
Aquamox with reserpine tabs (Lederle) (2nd, 1985)*†
Aristocort tabs 2 mg (Lederle) (3rd, 1985)†‡
Ascofer (Desbergers)
Asthmophylline elixir (Sabex)
Atasol-8, -15 & -30 tabs (Horner)
AVC Dienestrol suppositories (Merrell)
AVC suppositories (Merrell)
Aventyl caps 10 & 25 mg (Lilly)‡§
Azosulfizole tabs (ICN)
B & C caps (ICN)
Beforte tabs (Frosst)
Bellergal Spacetabs (Sandoz)
Bellergal tabs (Sandoz)
Benzedrine tabs 5 mg (SK & F)
Bilopaque (Winthrop)
Bilron caps (Lilly)‡§
Bio-Minal (Fréga)
Biosan caps 250 & 500 mg (ICN)
Bisacodyl tabs 5 mg (Sands)
Bisacolax tabs 5 mg (ICN)
Bradosol green lozenge (Ciba)
Bradosol yellow lozenge (Ciba)
Broncho-Grippol-DM syrup (Charton)
Cafergot-PB tabs (Sandoz)
Campain elixir (Winthrop)
Campain pediatric drops (Winthrop)
Carbolith caps 300 mg (ICN)
Carbrital caps (Parke-Davis)‖
Carbrital half-strength caps (Parke-Davis)‖
Cardialine caps (Fréga)
Cascara tabs 300 mg (Drug Trading)
Cascara Sagrada tabs 200 mg (Parke-Davis)
Cefracycline tabs (Frosst)
Cēpacol anesthetic discs (Merrell)
Cēpacol mouthwash/gargle (Merrell)
Cēpacol throat lozenge (Merrell)
CES tabs (ICN)
Children's chewable vitamins (Drug Trading)
Chloral hydrate caps 500 mg (Drug Trading)
Chloralvan caps (ICN)
Chlordiazepoxide caps 5, 10 & 25 mg (Drug Trading)
Chlordiazepoxide caps 5, 10 & 25 mg (Sands)
Chlorpheniramine maleate tabs 4 mg (Sands)
Chlorprom tabs (ICN)
Choloxin tabs 2 & 6 mg (Flint)
Citro-Mag (Rougier)
Clomid tabs 50 mg (Merrell)
Cloxapen caps (ICN)¶
Cloxilean caps 250 & 500 mg (Harris)
Co-Actifed tabs (BW Inc.)
Colchicine tabs 0.6 mg (Welcker-Lyster)
Colchine tabs 0.6 mg (Drug Trading)
Cold & decongestant tabs (Drug Trading)
Coldecon Plus caps (Parke-Davis)
Combid Spansule caps (SK & F)
Conjugated estrogen tabs 1.25 mg (Sands)
Contac C caps (Menley & James)
Cophylac drops (Hoechst)
Cophylac expectorant drops (Hoechst)
Co-Pyronil caps (Lilly)‡§
Corax caps (ICN)
Cordex Forte Improved tabs (Upjohn)
Cordex Improved tabs (Upjohn)
Cough suppressant syrup (Drug Trading)
Cuprimine caps (MSD)
Cyclex tabs (MSD)
Cyclospasmol tabs 200 & 400 mg (Wyeth)
Cynax (500 mg artichoke ext.) (Québeurope Import)
Cystex tabs (Cooper)
Dalmane caps 30 mg (Roche)‡§
Daltose-100 & -200 tabs (Nordic)
Decadron tabs 0.5 & 0.75 mg (MSD)
Declomycin FC tabs 150 mg (Lederle) (2nd, 1986)†‡
Declomycin FC tabs 300 mg (Lederle) (1st, 1984)†‡
Decongestant syrup (Drug Trading)
Demure cleansing deodorant douche (Vick Chem)
Dequadin lozenge (lemon) (Glaxo)
Dexasone tabs 0.5 mg (ICN)
Dexedrine Spansule caps 10 & 15 mg (SK & F)
Dexedrine tabs (SK & F)
Dilantin Infatabs (Parke-Davis)
Dilantin with phenobarbital caps 30 mg (Parke-Davis)
Dimedrine tabs (Robins)
Dimelor tabs (Lilly)‡§
Dimetapp-DM tabs (Robins)
Donnatal Extentabs (Robins)
Donnazyme tabs (Robins)
Dopamet tabs (ICN)
Dramamine tabs (Searle)
Drops-Ear-analgesic (Drug Trading)
Dual Action cough drops cherry flavour (Vick Chem)
Ducolax tabs 5 mg (Boehringer)
Dynapen oral susp. (Bristol)
Earache drops (Drug Trading)
ECT ASA tabs 650 mg (Drug Trading)
Elavil tabs 25 & 50 mg (MSD)
Elixin creosote & terpin hydrate compd. (Drug Trading)
Eltor liquid (Dow)
Eltroxin tabs 100 & 300 μg (Glaxo)
Emetrol solution (Rorer)
Energex Fort (Fréga)
Enovid tabs 10 mg (Searle)
E-Pam tabs 5 mg (ICN)
Ergodryl caps (Parke-Davis)
Esidrix tabs 50 mg (Ciba)
Everyday multiple vitamins (Drug Trading)
Everyday multiple vitamins with iron (Drug Trading)
ExNa tabs (Robins)
Falapen tabs (Frosst)
Fem iron tabs (Williams)
Ferrofume (Nordic)
Ferrous gluconate tabs (ICN)
Ferrous gluconate tabs 300 mg (Drug Trading)
Ferrous sulphate tabs (ICN)
Fertinic C (Desbergers)
Fesofor tabs (SK & F)
Flintstones lemon & lime flavours (Miles)#
Fluorinse 0.2% mint (Cooper)
Fluotic-20 (Nordic)
Folvit tabs 5 mg (Lederle) (2nd, 1985)*†
Food or fruit colouring green (Drug Trading)
Forhistal 1 mg (Ciba)
Formule Ner (Fréga)
Fortamines 10 caps (Rougier)
Fregalex (Fréga)
Furoside tabs (ICN)
Gel-ll butterscotch (Cooper)
Gel-ll lemon (Cooper)
Geritol tabs (Williams)
Geviral tabs (Lederle) (1st, 1982)†‡
Glysennid 12 mg (Anca)
Gravol liquid (Horner)
Gravol tabs (Horner)
Haldol tabs 5 & 10 mg (McNeil)
Halotestin tabs 5 mg (Upjohn)
Hip-Rex tabs (Riker)
Histalon tabs (ICN)
Hycodan-E syrup (Endo)
Hycomine syrup (Endo)
Hycomine-S syrup (Endo)
HydroDIURIL tabs 100 mg (MSD)
Hydropres-25 & -50 mg tabs (MSD)
Hygroton tabs 50 mg (Geigy)
Ilosone caps (Lilly)‡§
Ilosone chewable (Lilly)‡§
Ilosone tabs (Lilly)‡§
Imipramine HCl tabs 10, 25 & 50 mg (Drug Trading)
Imipramine tabs 10, 25 & 50 mg (Sands)
Impril tabs 10, 25 & 50 mg (ICN)
Intal-p caps (Fisons)**
Iodaminol 10 (Desbergers)
Ionamin caps 30 mg (Pennwalt)††
Ismelin tabs 10 mg (Ciba)
Isotamine-B-300 tabs (ICN)
Kalium Durules (Astra)‡‡
KCL 20% (Rougier)
Keflex caps 250 mg (Lilly)‡§
Keflex tabs 250 & 500 mg (Lilly)‡§
Kérabec composé (Rougier)
Kérabec simple (Rougier)
KI tabs (Rougier)
Lanoxin tabs 0.125 mg (BW Inc.)
Largactil liquid 100 mg/5 ml (Rhône-Poulenc)
Lasix tabs 40 & 80 mg (Hoechst)
Lasix oral solution (Hoechst)
Lasix Special tabs 500 mg (Hoechst)
Lecithin with D caps (Swiss Herbal)
Lederon caps (Lederle) (3rd, 1982)†‡§§
Lemon Time (hot lemon drink) (Buckley)
Levazine 4/25 tabs (ICN)
Librium caps 5 & 25 mg (Roche)‡§
Limonade Asepta (Rodeca)
Limonade Rodeca (Rodeca)
Linodil (Winthrop)
Lipoflavonoid caps (Cooper)
Listerine lozenges — lemon mint flavour (Warner-Lambert)
Livertal (Fréga)
Loestrin 1.5/30 tabs, inert tabs only (Parke-Davis)
Loxapac tabs 5 mg (Lederle) (2nd, 1983)*†
Loxapac tabs 10 mg (Lederle) (2nd, 1984)*†
Ludiomil 25 mg (Ciba)
Maalox Plus LSC tabs (Rorer)
Madribon susp. (Roche)
Madribon tabs (Roche)
Mebroin (Winthrop)
Megacillin 250 susp. (Frosst)
Menrium tabs 5-2 & 5-4 (Roche)
Mentholatum medicated lozenge (natural flavour) (Mentholatum)
Mephyton tabs (MSD)
Metandren Linguets 10 & 25 mg (Ciba)
Methaqualone HCl caps 300 mg (Bio-Chem)
Methidate tabs 20 mg (ICN)
Methotrexate tabs 2.5 mg (Lederle) (2nd, 1986)*†

Methyldopa tabs 125, 250 & 500 mg (Drug Trading)
Methyldopa tabs 125, 250 & 500 mg (Sands)
Methylergobasine-Sandoz tabs (Sandoz)
Mi-Cebrin tabs (Lilly)‡§
Mi-Cebrin T tabs (Lilly)‡§
Minocin caps 50 mg (Lederle) (2nd, 1982)†‡
Minocin caps 100 mg (Lederle) (1st, 1983)†‡
Modacon (28 day) green placebo tabs (Ortho)
Moditen HCl tabs 2 mg (Squibb)
Multicebrin tabs (Lilly)‡§
Multiple vitamin and mineral tabs (Drug Trading)
Myadec caps (Parke-Davis)‡§
Mycostatin oral tabs 500 000 IU (Squibb)
Nadopen-V tabs (Nadeau)
Nadozone (Nadeau)
Nalfon caps 300 mg (Lilly)‡§
Nalfon tabs 600 mg (Lilly)‡§
Natulan caps (Roche)‡§
Naturetin 2.5 & 5 mg (Squibb)
Naturetin-K 5 mg (Squibb)
Nervosyl (Fréga)
Neuro-Trasentin (Ciba)
Nikoban lozenges mint (Williams)
Nilstat oral drops (Lederle) (2nd, 1984)*†
Nitrofurantoin tabs 50 & 100 mg (Drug Trading)
Nobesine-75 (Nadeau)
Norlestrin 1/50 tabs (Parke-Davis)
Norlutate tabs (Parke-Davis)
Norlutan tabs (Parke-Davis)
Norpramin 50 & 75 mg (Merrell)
Noscatuss syrup (Fisons)††
Novahistex liquid (Dow)
Novahistex tabs (Dow)
Novahistine liquid (Dow)
Nozinan tabs 5, 25 & 50 mg (Rhône-Poulenc)
Nyquil Nighttime Cold Medicine (Vick Chem)
Osetrilin 0.625, 1.25 & 2.5 mg (Desbergers)
Oestrilin-Testo-Pheno (Desbergers)
One Daily chewable tabs (ICN)
One Daily with iron tabs (ICN)
Oragrafin sodium caps 500 mg (Squibb)
Orap 4 mg (McNeil)
Orenzyme tabs (Merrell)
Organol 39 (Fréga)
Orifer (Dow)
Ortho-gynol contraceptive jelly (Ortho) (2nd, 1986)††
Ortho-Novum 1/35-28 d (green placebo tabs) (Ortho)
Ortho-Novum 1/50 tabs (Ortho)
Ortho-Novum 1/50-28 d (green placebo tabs) (Ortho)
Orudis cap 50 mg (Rhône-Poulenc)
Oxpam tabs 10 & 15 mg (ICN)
P-50 liquid (Horner)
Panectyl liquid 2.5 mg/5 ml (Rhône-Poulenc)
Panteric tabs (Parke-Davis)
Pardec chocolate chewable tabs (Parke-Davis)
Pathibamate tabs 400 mg (Lederle) (1st, 1985)†
Pentobarbital sodium caps 100 mg (Drug Trading)
Percodan tabs (Endo)
Periactin syrup (MSD)
Peritrate tabs 20 mg (Parke-Davis)
Peritrate SA tabs 80 mg (Parke-Davis)
Peritrate Forte (Parke-Davis)
Pertofrane (Geigy)
Phenaphen No. 3 & 4 caps (Robins)
Phenazo tabs 100 mg (ICN)
Phenbuff caps (Sands)
Phenbutazone tabs (ICN)
Phenobarbital tabs 15, 30 & 50 mg (Bio-Chem)
Phenobarbital tabs 30 & 60 mg (ICN)
Phenoxene 50 mg (Dow)
Phenylbutazone tabs (Sands)
Plexonal Forte tabs (Sandoz)
Polyfer (Fréga)
Polymine No. 2 (Fréga)
Polymox caps 250 & 500 mg (Bristol)
Polymox 125 & 250 mg/5 ml susp. (Bristol)
Ponderal Pacaps (Servier)
Potassium citrate & hyoscyamus (Drug Trading)
Praminil 10, 25 & 50 mg (Nordic)
Prednisolone tabs 5 mg (Drug Trading)
Pro-65 caps (ICN)
Pro-Biosan kit (ICN)
Proco-65 caps (ICN)
Program 20 tabs (Ortho)
Prolopa caps 100-25 & 200-50 (Roche)
Promaquid caps 20 mg (Rhône-Poulenc)
Promazine HCl tabs 25 & 50 mg SCT (Drug Trading)
Pronestyl caps 250 & 500 mg (Squibb)
Propanthel tabs 15 mg (ICN)
Prosedyl tabs (Rougier)
Prostalgine suppositories (Nova)
Prostaphlin caps 250 & 500 mg (Bristol)
Provera tabs 5 mg (Upjohn)
PVF suspension 150 & 300 mg (Frosst)
Pyr-Pam tabs (ICN)
Quide 10 & 25 mg (Dow)
Quinine caps 200 & 300 mg (Parke-Davis)‖
Raudixin tabs 50 & 100 mg (Squibb)
Rautractyl-2 (Squibb)
Rautractyl-4 (Squibb)
Revit Plus caps (ICN)
Revitonus C-1000 (Sabex)
Ritalin 20 mg (Ciba)
Robimycin tabs (Robins)
Rofact caps 300 mg (ICN)
Roniacol Supraspan tabs 150 mg (Roche)
Rouqualone (Rougier)
Rovamycine caps 250 & 500 mg (Rhône-Poulenc)
Rythmodan caps 100 mg (Roussel)‡
Sandomigran tabs 0.5 mg (Sandoz)
Sansert tabs (Sandoz)
Seconal sodium caps 50 & 100 mg (Lilly)‡§
Serax tabs 10 & 15 mg (Wyeth)
Serpasil-Esidrix 25 & 50 mg (Ciba)
Solatene caps (Roche)
Solazine tabs 1 mg (Horner)
Sopalamine-3B (Nordic)
Sopalamine-3B plus C (Nordic)
Sparine tabs 25 mg (Wyeth)
Spec-T (orange) lozenge (Squibb)
Stelazine concentrate (SK & F)
Stemetil caps "spans" 10 mg (Rhône-Poulenc)
Stemetil tabs 5 & 10 mg (Rhône-Poulenc)
Sterazolidin (Geigy)
Stibilium 5 mg (Desbergers)
Stilboestrol tabs 1 mg (Glaxo)
Stress-Pam tabs 5 mg (Sabex)
Stresscaps (Lederle) (2nd, 1984)*†
Stresscaps 600 (Lederle) (2nd, 1984)*†
Sulfarlem-choline tabs (Charton)
Sulla tabs (Robins)
Supres tabs 150 & 250 mg (Frosst)
Survit-Plus (ICN)
Symmetrel caps (Endo)
Synthroid tabs 0.1 & 0.3 μg (Flint)
Tabron tabs (Parke-Davis)
Tace caps 12, 25 & 72 mg (Merrell)
Tarasan tabs 15 & 50 mg (Roche)
T-Caps 250 mg (ICN)
Tegopen caps 250 mg (Bristol)
Tenuate tabs 25 mg (Merrell)
Terfluzine concentrate 10 mg/ml (ICN)
Terpo-Dionin (Winthrop)
Tetracycline caps & tabs 250 mg (Sands)
Tetrex caps 500 mg (Bristol)
Theolixir (ICN)
Thioridazine tabs 25 & 100 mg (Drug Trading)
Thioridazine tabs 10, 25 & 100 mg (Sands)
Thioril tabs 10, 25 & 100 mg (ICN)
Throat Aids (Buckley)
Throat lozenges (Drug Trading)
Thyroid tabs 100 mg (Parke-Davis)
Torecan tabs (Sandoz)
Tracinet troches (MSD)¶
Trancopal (Winthrop)
Triaminic AC (Anca)
Trifluoperazine HCl tabs 1, 2 & 5 mg (Drug Trading)
Trifluoperazine tabs 1.18, 2.36, 5.9 & 11.8 mg (Sands)
Tri-Vi-Flor chewable tabs (Mead Johnson)
Tri-Vi-Sol chewable tabs (Mead Johnson)
Trulfacillin suspension 3-200 & 7½-300 (Frosst)
Tualone-300 mg (ICN)
Tussionex susp. (Pennwalt)
Tutamate BF tabs (Frosst)
Urecholine tabs 25 mg (Frosst)
Uridon tabs 50 mg (ICN)
Valda (Rodeca)
Valpin PB tabs (Endo)
Varicyl (Nadeau)
VC-K Pediatric (Lilly)‡§
Velosef caps 500 mg (Squibb)
Venoplant (Nordic)
Viamon (Nadeau)
Vicks lemon throat drops (Vick Chem)
Victors Medicated "Vapo-lyptus" (Vick Chem)
Vi-met syrup (Nordic)
Vimicon syrup (Frosst)
Vitamin B compound with C tabs (ICN)
Vitamin B compound with C Fortis caps (Drug Trading)
Vitamin C chewable tabs 100, 250 & 500 mg (Drug Trading)
Vitamin E caps 100, 200 & 800 IU (ICN)
Vitathion (Servier)
Vivol 2, 5 & 10 mg tabs (Horner)
Vontrol tabs (SK & F)
Warfilone tabs (Frosst)
Zarontin caps (Parke-Davis)
Zaroxolyn tabs 10 mg (Pennwalt)
Z-BEC tabs (Robins)
282 tabs (Frosst)
642 tabs (Frosst)

*Expected to change to tartrazine-free formula by the second quarter of 1981.
†Expecting to remove tartrazine product from retailers' shelves by quarter and year in parenthesis.
‡Present formula is without tartrazine.
§Product on retailers' shelves may contain tartrazine.
‖Capsule imprinting ink only. Currently phasing in new ink without tartrazine.
¶Discontinued.
#Flavour discontinued January 1981.
**Tartrazine in coloured end of capsule only. This end is not pierced, and there is no leaching of tartrazine into capsule contents.
††Some batches may contain tartrazine, depending on supplier of capsule shells.
‡‡Current batch contains tartrazine; new batches will not contain tartrazine.
§§Two products are marketed — one with and the other without tartrazine.

Survey of drug manufacturers

Methods

To identify the Canadian drug products that presently contain tartrazine, a form letter was mailed in January 1981 to 253 pharmaceutical companies listed in the 1980 editions of the "Compendium of Pharmaceuticals and Specialties" (CPS) and "Canadian Self-Medication," a handbook of over-the-counter drugs. The company officials were asked to indicate which of the products they manufacture or distribute in Canada contain tartrazine. Officials of companies that apparently did not use tartrazine in any of their products were asked to verify that they did not.

Results

Most replies were received by April 1981. Of the 135 (53.4%) pharmaceutical manufacturers who responded approximately 39% indicated that none of their drug products contained tartrazine; these companies are listed in Table I. Companies who indicated that tartrazine was being completely phased out of their drug formulations and who gave dates for these changes are also included in Table I.

From the responses of the other manufacturers who indicated that one or more of their drug products intended for oral use contained tartrazine a list of approximately 450 tartrazine-containing drug products was compiled (Table II). Some of the products listed are being reformulated: a company may have removed tartrazine from a formulation, but batches currently on retailers' shelves may contain the dye. Details on expected dates of these changes are included in Table II. As with previous listings,[8,9,26,27] the information, obtained in the first quarter of 1981, will change as manufacturers continue to reformulate their products.

Discussion

Tartrazine is one of several agents included in drug formulations that may cause idiosyncratic reactions. In the general population the incidence of tartrazine sensitivity is low. Among asthmatic and allergic individuals and those sensitive to ASA the incidence of tartrazine hypersensitivity is probably less than 20%. However, although the number of individuals at risk is small, the problem remains serious, as the reaction in those who are sensitive may be anaphylactoid.

The drug products listed in Table II are of many therapeutic classes and include some that are commonly administered to asthmatic and allergic persons: theophylline preparations, antibiotics, corticosteroids, antihistamines and antihistamine–decongestant combinations. Physicians should be aware that tartrazine is contained in certain drug products so that they can avoid prescribing these products to those who are known to be tartrazine-sensitive or to those who may be at risk of such a reaction. The presence of tartrazine in some antihistamine and corticosteroid products may explain the idiosyncratic reactions that some patients have to these drugs.

Since 1980, pharmaceutical manufacturers in the United States have been required to state on the label that a product contains tartrazine.[28] Prescription drugs requiring a package insert must also include this information in the "Precautions" section. These labelling requirements are the most thorough method of ensuring that drug products containing tartrazine are easily recognized. Listings of drugs are useful guides, but their completeness is limited and constant revision is required.

I recommend that the Canadian government join the Food and Drug Administration (FDA) in the United States in requiring drug products intended for oral use to be labelled as to tartrazine content. Requiring manufacturers to include this information in the monographs they supply to the compilers of the CPS and "Canadian Self-Medication" would be an additional safeguard.

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