Still too many analgesic mixtures

I
n the early 1980s many preparations sold over the counter in France contained up to eight active substances with various effects, such as nonsteroidal antiinflammatory drugs, caffeine, opiates, barbiturates and antihistamines.

“Anti-mixture” measures in 1982. Work by the French health authorities led to welcome but partial changes in composition, such as the withdrawal of amiodopyrine (a pyridine derivative), prescription drug status for noramiodopyrine (risk of agranulocytosis) and phenacetin (an antipyretic analgesic carrying a risk of nephropathy, haemolytic anaemia and methaemoglobinemia); and a total dose limit of 8 grams for boxes of paracetamol (to reduce the risk of liver damage after overdose) (1-4).

Further improvements in the 1990s. The composition of some analgesic-based preparations has since been further simplified, such as the gradual disappearance of phenacetin (5); barbiturates (6,7); butabital (8); quinine derivatives (9); and clearance of bromide from one product (10,11,12). Note that these changes often consisted of replacing one substance with another, considered less harmful (paracetamol replacing phenacetin, for example).

The French medicines agency era: bad analgesic mixtures still on the market. Analogous combinations containing three or even four active substances are still on the French market, usually with authorisations decades old. It is well known that these combinations have a negative risk-benefit balance, notably because of additive adverse effects, drug interactions, and risks associated with concurrent intake of another preparation containing the same substances.

Several obsolete substances are still available, such as belladonna powder combined with codeine, caffeine and paracetamol, and opium powder combined with paracetamol and caffeine. Caffeine is ubiquitous, despite the lack of proven analgesic effects and the known risks of excitatory and anxiogenic effects (13). Examples are products containing caffeine combined with aspirin and paracetamol; aspirin and meadow queen (Filipendula maria); paracetamol and codeine; paracetamol and dextropropoxyphene; aspirin and codeine; and a “homeopathic” product containing tinctures of belladonna and other substances combined with standard doses of aspirin and caffeine.

These mixtures have numerous disadvantages, including a risk of additive adverse effects and interactions; different regulatory statuses; risks of interactions with dietary components (especially alcohol and caffeine); various trade names bearing little relevance to the nature of the components; and uninformative packaging (international non proprietary names mentioned in small print on the side of the box but not on the blister); and incoherent patient information leaflets.

The French medicines agency seems simply to ignore these facts, doing nothing to withdraw these mixtures from the market.

European measures to be applied in France. European Directive 2004/27/EC stipulates that fixed-dose combinations containing up to three active substances must mention all three international non proprietary names on the outer and inner packaging (14). And, hopefully, the new obligation that information leaflets be tested on panels of potential users will further underline the incoherence of such mixtures.

*Prescrire*