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## Case report

### Ketoprofen contact dermatitis with good pikeprofen tolerance

Ketoprofen, like pikeprofen, is a non-steroidal antiinflammatory drug belonging to the arylpropionate pharmacological family, and they both have similar structures. We report the case of a patient who developed contact eczema on the left hand and wrist after the topical application of a ketoprofen-containing gel; the patient later tolerated the application of another gel containing pikeprofen. The allergological studies confirmed sensitisation to ketoprofen and tolerance to pikeprofen. This case confirms that in the contact dermatitides due to non-steroidal antiinflammatory drugs sensitisation it is not always necessary to prohibit the use of all the drugs in the pharmacological group of the one causing the reaction. An allergological study is advisable in order to establish which drugs should be avoided.

**Key words:** Dermatitis. Ketoprofen. Pikeprofen.

### Dermatitis de contacto por ketoprofeno con buena tolerancia de pikeprofeno

El ketoprofeno es un antiinflamatorio no esteroideo perteneciente a la familia de los arilpropiónicos, al igual que el pikeprofeno, que presenta una estructura similar. Se presenta el caso de un varón de 41 años que sufrió un eccema de contacto en muñeca y mano izquierdas tras la aplicación tópica de un gel que contenía ketoprofeno; el paciente toleró posteriormente la aplicación de un gel con pikeprofeno. El estudio alergológico demostró la sensibilización del paciente a ketoprofeno y la tolerancia de pikeprofeno. Se concluye que en las dermatitis de contacto por sensibilización a antiinflamatorios no esteroideos, no siempre es necesario prohibir al paciente todos los fármacos pertenecientes al mismo grupo del causante de la reacción, y es recomendable un estudio alergológico para concretar los fármacos que deben evitarse.

**Palabras clave:** Dermatitis. Ketoprofeno. Pikeprofeno.

**K**etoprofen (Fig. 1) is a non-steroidal antiinflammatory drug (NSAID) belonging to the arylpropionate family, which is widely used in the topical form. Pikeprofen has a similar structure, in which an OH radical has been substituted with an amido one bound to a pyridine group (Fig. 2). They are both widely used in topical preparations for rheumatologic conditions and musculoskeletal traumatism.

A bibliography investigation in the MEDLINE (1966 - 2000) and EMBASE (1974 - 2000) databases and in the Revista Española de Alergología

e Inmunología Clínica has yielded several cases of contact dermatitis<sup>1-6</sup> and photodermatitis<sup>7-12</sup> caused by ketoprofen, as well as one case of contact dermatitis due to piketoprofen<sup>13</sup> and a further one of contact photodermatitis due to ketoprofen and piketoprofen<sup>14</sup>. There are a number of published cases of cross-reactivity between ketoprofen and other arylpropionate NSAIDs such as ibuprofen<sup>15</sup>, flurbiprofen and thiaprofenic acid<sup>8,11</sup>.

We report the case of one patient who consulted because of an important local reaction after the application of a ketoprofen-containing gel.

## CASE REPORT

A 41-year-old male reported that, some four years earlier and upon applying Fastum Gel® (ketoprofen, ethyl alcohol, carbomer, diethanolamine, essence of lavender, methyl *para*-hydroxybenzoate, propyl *para*-hydroxybenzoate) topically onto his left wrist, he evidenced, some eight hours later and with no relation to sunlight exposure, skin erythema on the area of application which then spread to the whole left hand with blebbing and later desquamation. This episode persisted for 15 days and required therapy with oral antihistamines and topical corticosteroids.

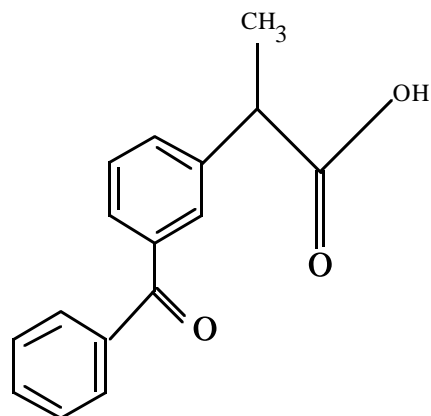
Later on, the patient had used on various skin areas topical Calmatel Gel® (piketoprofen, propyl-cellulose hydroxide, propylenglycol, essence of lavender, ethyl alcohol), with good tolerance.

### Allergy study

Skin prick tests were performed with a panel of airborne allergens prevalent in our environment (moulds, house dust mites, animal epithelia and danders, and pollens), with negative results.

Epicutaneous testing with a standard contact allergen panel (True Test®, ALK-Abelló) also yielded negative results.

Epicutaneous tests were then performed with the components of the Fastum Gel® preparation (ketoprofen, ethyl alcohol, carbomer, diethanolamine, essence of lavender, methyl *para*-hydroxybenzoate, propyl *para*-hydroxybenzoate) and with piketoprofen. The test was positive at the 48 and 96-hour readings, for 2% ketoprofen in vaseline, with erythema, infiltration and some microvesicles (+++) (Fig. 3), and negative for piketoprofen



3-benzoyl- $\alpha$ -methyl-benzene-acetic acid (C<sub>16</sub>H<sub>14</sub>O<sub>3</sub>)  
PM = 254.29

Fig. 1. Ketoprofen.

and for the remaining tested components of Fastum Gel®.

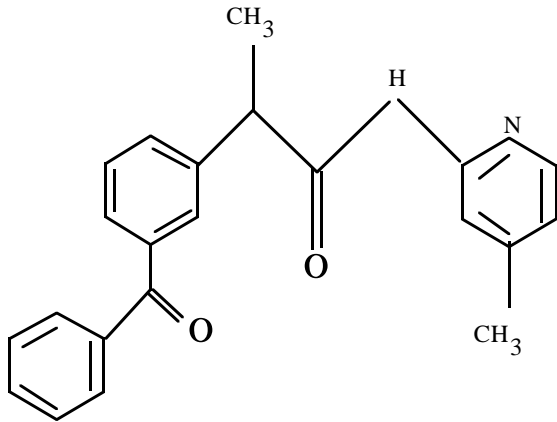
In order to assess the oral tolerance to other arylpropionate NSAIDs, an oral challenge test with increasing doses of ibuprofen (up to 600 mg) with negative result.

The patient reported full oral tolerance of paracetamol and acetylsalicylic acid, so that no further oral challenge tests with other NSAIDs were performed.

## DISCUSSION

Ketoprofen is a non-steroidal antiinflammatory drug of the arylpropionate group, widely used in topical preparations, which has a considerable sensitising potential. There are reports in the literature of a sizeable number of cases of ketoprofen contact dermatitis<sup>1-6</sup> and photodermatitis<sup>7-12</sup>. Moreover, in some patients, cross-reactivity has been demonstrated between ketoprofen and other NSAIDs of the same pharmacological group such as ibuprofen, flurbiprofen and thiaprofenic acid<sup>8</sup>, as well as between ketoprofen and other molecules containing a benzophenone moiety such as fenofibrate<sup>11,16</sup> and between ketoprofen and fragrance mixes mainly cinnamic aldehyde and Peru balsam<sup>17</sup>.

The patient here reported evidenced contact dermatitis due to ketoprofen sensitisation but tolerated another similar NSAID, piketoprofen, also belonging to the arylpropionate family; cross-reactivity between the two drugs has already been reported<sup>14</sup>.



3-Benzoyl- $\alpha$ -methyl-N-(4-methyl-2pyridinyl) bencenoacetamida ( $C_{22}H_{20}N_2=2$ )  
MW = 344.41

Fig. 2. Piketoprofen.

The two drugs share a similar structure, in which the terminal  $-\text{COOH}$  radical of ketoprofen (Fig. 1) has been replaced by an amido one bound to a pyridine ring in piketoprofen (Fig. 2). It is open to speculation whether this substitution modifies the antigenic structure of the drug or whether, as they are both low-molecular weight compounds behaving as haptens, the loss of the terminal carboxyle radical might modify their ability to bind to dermal proteins, so that piketoprofen would be less sensitising than ketoprofen.

As demonstrated by the present case, and despite the cross-reactivity potential between ketoprofen and other non-steroidal antiinflammatory drugs of the same pharmacological group, when a contact dermatitis caused by sensitisation to one of these drugs is encountered it is not always necessary to forbid the patient to use all the drugs of the same pharmacological group as the one causing the index reaction. In these cases, it is advisable to carry out epicutaneous tests with several of these drugs, so as to assess the patient's degree of sensitisation.

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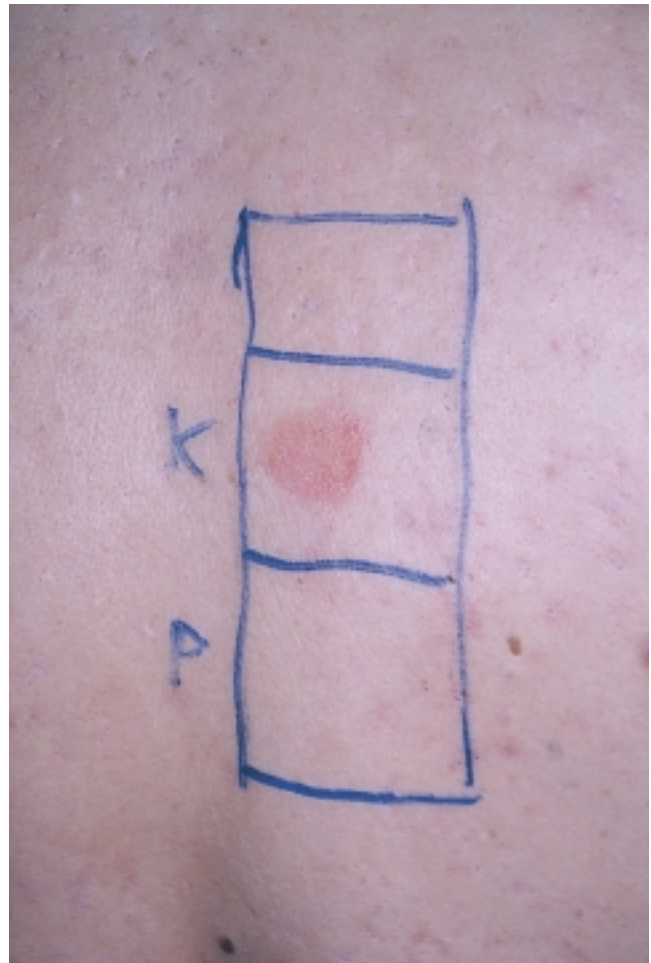


Fig. 3.

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