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CONTROVERSIES IN THE CONDUCTING OF DRUG PATCH TESTING

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BACKGROUND

The drug patch test (DPT) is useful as a tool for diagnosing delayed hypersensitivity skin reactions to medications. However, there is no consensus on concentration and vehicle for testing, which justifies the need to standardize a conducting method.

PURPOSE

To describe a method of preparation of DPTs from active ingredients (AI) commercialized as drugs as well as pure substances, to unify available information and to add our experience, so providing a methodology for those AI not described in current literature.

PATIENTS AND METHODS

Retrospective analysis of DPTs performed in the Hospital Pharmacy Department of a 300-bed hospital over a period of 50 months.

- For those **AI** in which **information** was **available** at the moment of the study, the patch was prepared according to the concentration and vehicle described in the literature. In those cases where there was no agreement about the vehicle to choose, it was selected according to the solubility of the AI in water.
- For those **AI not described in the literature**, the development of the test depended on the concentration to be tested, the formulation of the drug and the choice of vehicle.

RESULTS

122 AI and 178 types of DPTs were tested, with a total of 377 DPTs prepared.

For 55.8% of the tested AI, there was no clear information on concentration and vehicle at the moment of its preparation; currently, this information does not exist in 36.9% of tests requested.

A total of 72.1% of DPTs were prepared in petrolatum (AI insoluble/poorly soluble in water).

For 27.3% of the AI for which there was information about procedure of preparation, there was controversy about whether to use the commercialized drug or pure allergen.

- The **mean concentration of AI in the starting drug** was 39% (median 25%). Twenty-nine percent of drugs contained ≤10% AI (≥50% AI: 35% of the drugs).
- The **mean concentration of AI in DPT** was 59% (median: 1.8%). A total of 50.1% of DPTs tested had an AI concentration ≤2%.

Table 1. Active ingredients (AI) in drug pacht tests (DPTs) described in the literature

AI tested	Registered trade name	DPT tested	DPT described in the literature	Water solubility of the AI
Acetaminophen	Termalgin® 500 mg tablet	5%; 10%; 30% HV	10%*(vehicle ND)[9] 30% pet./aq./alc.[10] 30% pet.[11] 10% pet.*,[12]	1.4 g/100 ml: very slightly soluble in cold water[a]
Acetylsalicylic acid	Tromalyt® 150 mg capsule	2%; 10% pet.	2%,10% pet.[5] 10% (vehicle ND)[9] 1%, 10% vas*,[12]	0.46 g/100 ml: Poorly soluble[a]
Acyclovir	Aciclovir Combino Pharm® 250 mg injectable form	5% pet./alc.	1-5% pet.; 5% aq../alc. 10%* pet.[11]	
Allopurinol	Zyloric® 100 mg tablet	10%; 30% pet.	30% pet./aq./alc.[10] 10%, 20% pet.*,[12]	
Alprazolam	Alprazolam Cinfa® 2 mg tablet	30% pet.	30% pet./aq./alc.[10]	
Amoxicillin	Amoxicilina Normon® 500 mg tablet	1%; 10%; 20% pet.	20%[8] 30% pet.[10] 10%* pet.[11] 5%* (vehicle ND)[9] 1%, 10%, 20%* pet.	
Amoxicillin-clavulanic acid	Amoxicilina-clavulánico Normon® 500 mg	30% pet.	30% pet./aq./alc.[10]	

Table 3. Concentrations of active ingredients (AI) in drug and in drug patch tests (DPTs).

Tested DPT	Concentration of AI in drug (%)	Concentration of AI in DPT (%)
Acenocoumarol 30%	0.7%	0.2%
Acetaminophen 5%; 10%; 30%	73.5%	3.7%; 7.4%; 22.1%
Acetylcysteine 30%	19.6%	5.9%
Acyclovir 5%	100%	5%
Acetylsalicylic acid 2%; 10%	79%	1.6%; 7.9%
Allopurinol 10%; 30%	32.7%	3.3%; 9.81%
Alprazolam 30%	0.8%	0.2%
Amlodipine 30%	2.5%	0.8%
Amoxicillin 1%; 10%; 20%	88.8%	0.9%; 8.9%; 17.8%
Amoxicillin-clavulanic acid 30%	10%	3%
Ampicillin 1%; 5%	100%	1%; 5%
Atenolol 30%	22.4%	6.7%

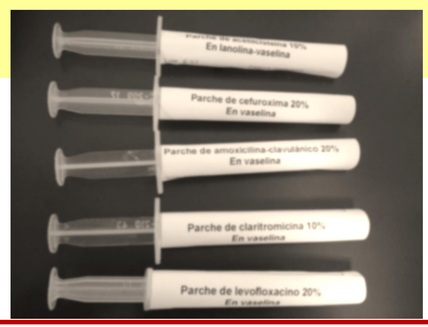

Table 2. Active ingredients (AI) in drug pacht tests (DPTs) not described in the literature.

AI tested	Registered trade name	DPT tested	Water solubility of the AI
Acenocoumarol	Sintron® 4 mg tablet	30% pet.	Insoluble[c]
Acetylcysteine	Acetilcisteina Normon® 200 mg tablet	30% HV	Soluble[c]
Amlodipine	Astudal® 10 mg tablet	30% pet.	0.008 g/100 ml: Insoluble[a]
Atorvastatin	Atorvastatina Normon®10 mg tablet	30% pet.	0.12 g/100 ml: Insoluble[a]
Bilastine	Bilaxten® 20 mg tablet	10%; 30% pet.	Insoluble[c]
Calcifediol	Hidroferol® 266 mcg injectable form	30% pet.	Insoluble[a]
Calcium glubionate	Calcium Forte Sandoz® 500 mg tablet	30% HV	Soluble[c]
Calcitriol	Calcitriol Kern Pharma® 1 mcg/ml injectable form	20% pet.	Insoluble[a]
Candesartan	Parapres® 32 mg tablet	1%;10%; 30% pet.	Insoluble[c]
Carvedilol	Coropres® 25 mg tablet	30% pet.	0.00006 g/100 ml: Insoluble[a]
Clorazepate dipotassium	Tranxilium® 50 mg tablet	15% HV	Very soluble[a]
Darbepoetin alfa	Aranesp® 30 mcg prefilled syringe	PURE	No information available
Dexketoprofen trometamol	Enantyum® 25 mg/ml injectable form	30% HV	Soluble[c]
Doxazosin	Doxazosina Cinfa® 4 mg tablet	30% pet.	Insoluble[c]
Ebastine	Ebastina Teva® 20 mg tablet	1% pet.	Insoluble[c]
Enalapril	Enalapril Normon® 20 mg tablet	20% HV	2.5 g/100 ml: Moderately soluble[a]
Febuxostat	Adenuric® 80 mg tablet	10% pet.	Insoluble[c]
Fexofenadine	Fexofenadina Sanofi® 180 mg tablet	10% pet.	Poorly soluble[a]
Furosemide	Seguril® 40 mg tablet	5% pet.	0.006 g/100 ml: Insoluble[a]
Gabapentin	Gabapentina Kern Pharma® 400 mg capsule	1%; 5% pet.	0.449 g/100 ml: Insoluble[a]

[a] Pharmacy codes; [b] Label sheet of the manufacturing company; [c] According to solubility of excipients; * Allergen supplied by the pharmaceutical industry (purity >95%).

AI: active ingredient; HV: hydrophilic vehicle; pet.: petrolatum; alc.: alcohol; Aq.: water; NS: Normal saline. ND: Not described concentration; M.P.: pure substance; mg: milligram; mcg: microgram; DMSO: Dimethylsulfoxide

CONCLUSIONS

This study presents action lines to improve the use of the patch test, highlighting the importance of conducting multicentre studies that standardize the procedures.