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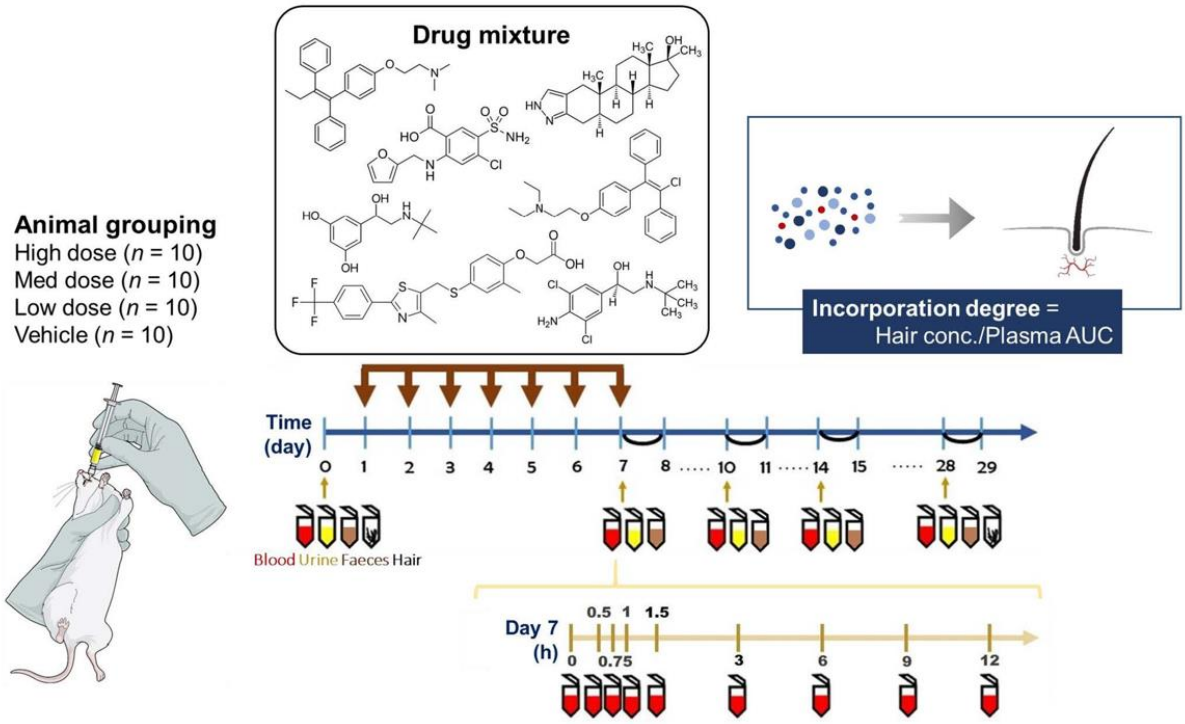
## 藥學院/藥學系

毛髮分析是法醫毒理學的一種重要方法，且在揭開運動員的用藥歷程方面具有潛在的應用價值。儘管它被廣泛應用，但對於毛髮中可檢測到的運動禁藥的認識仍然有限。本研究透過多方面方法評估毛髮檢體用於運動藥檢的可行性。通過動物模式比較 17 種模型藥物在不同基質中的劑量依存性和檢測時窗。利用 QSAR 模型，將動物實驗中的毛髮結合之數據外推到世界運動禁藥管制組織之清單上的所有物質。最後，以一項服用利尿劑和遮蔽劑之人體研究中進一步確認。

運動禁藥在血漿具有最佳的劑量依存性，但檢測時窗有限，而尿液、糞便次之，毛髮則最具回溯性，其中利尿劑之毛髮結合率最高，預測大多數同化性物質進入毛髮中，而胜肽荷爾蒙和乙二型致效劑等無法測得，可能是因其分子量大和高極性所致。而真實的人類頭髮研究通過分段分析證實這些利尿劑的施用時間。



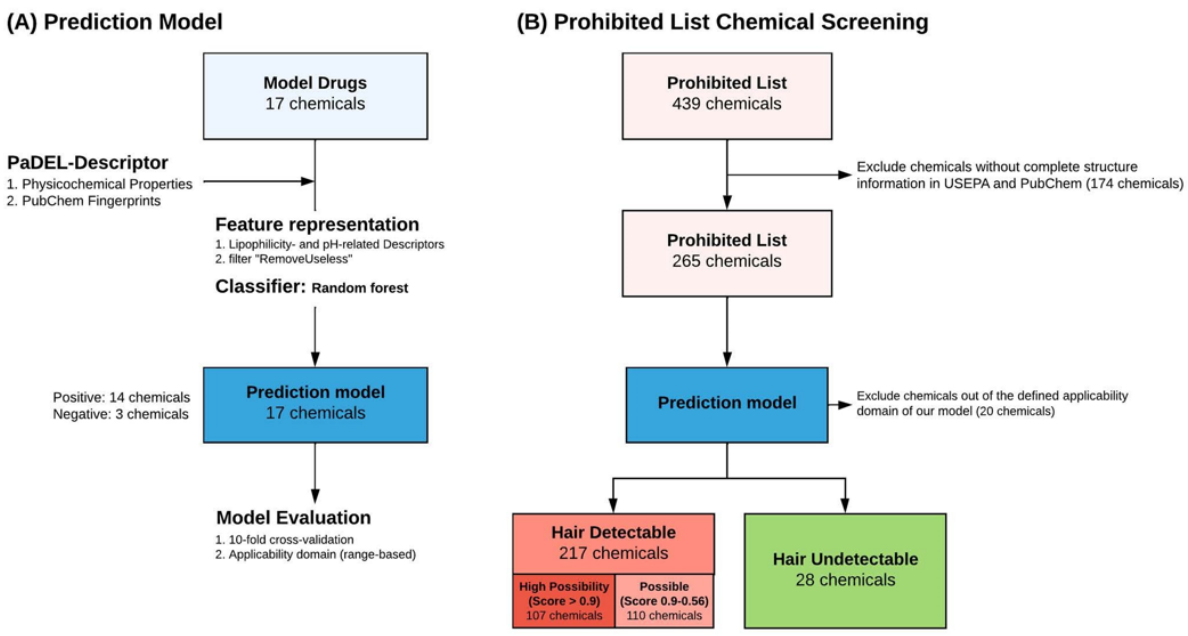




**Fig. 2** General workflow of in silico prediction for hair incorporation. **A** Quantitative structure–activity relationship model development and **B** screening result for substances on the prohibited list

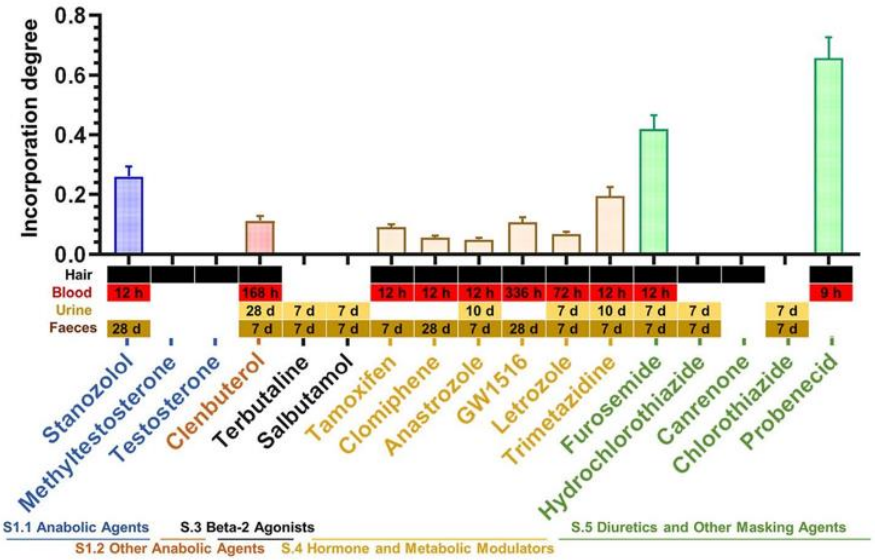



**Fig. 6** Hair incorporation degrees of substances in rats, calculated by dividing hair concentration by plasma AUC. Values are shown as the mean ± SEM for 30 rats. The grid below the column chart presents the detection windows of each substance between specimens

**Table 1** Drug distribution in hair samples obtained from subjects receiving diuretics and masking agents

| # | Drug | Duration (wk)* | Hair length (cm) 0–2 | 2–4 | 4–6 | 6–8 | 8–10 | 10–12 | 12–14 | 14–16 | 16–18 | 18–20 | 20–22 | 22–24 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| F1 | Letrozole | 100 | | | | | | | | | | | | |
| F2 | Furosemide | 96 | | | | | | | | | | | | |
| F3 | Furosemide | 1.5 | | | | | | | | | | | | |
| | Furosemide | 48 | | | | | | | | | | | | |
| F4 | Canrenone‡ | Unknown | | | | | | | | | | | | |
| | Hydrochlorothiazide | Unknown | | | | | | | | | | | | |
| M1 | Furosemide | 3 | | | | | | | | | | | | |
| | Canrenone‡ | 1 | | | | | | | | | | | | |
| F5 | Canrenone‡ | 5 | | | | | | | | | | | | |
| F6 | Hydrochlorothiazide | 5 | | | | | | | | | | | | |
| F7 | Hydrochlorothiazide | 26 | | | | | | | | | | | | |

F1: Female; Femara® 2.5 mg QD; Perm & Dye
F2: Female; Uretropic® 20 mg QD
F3: Female; Rasitol® 40 mg Q12H
F4: Female; Rasitol® 40 mg Q8H, Losa & Hydro® 50/12.5 mg QD, spironolactone 25 mg BID
M1: Male; Rasitol® 20 mg QD, Aldactone® 25 mg QD
F5: Female; Aldactone® 25 mg QD
F6: Female; Co-diovan FC® 80/12.5 mg QD; Perm & Dye
F7: Female; Sevikar HCT® 40/5/12.5 mg QD; Dye
*The duration of drug use prior to hair collection
†The colour scale represents the estimated drug concentration in hair segments, ranging 50–2600 pg/mg. Grey indicates not detected
‡The patients took spironolactone, and their hair was analyzed for canrenone, an active metabolite of spironolactone

【具體成果】

1. 利用少量的頭髮，將其分段分析即反映著運動員一整年的用藥史（若頭髮夠長），基於頭髮一個月約生長一公分，可精準得知藥物暴露的時間點。
2. 頭髮檢測幫助判斷運動員是長期蓄意施用運動禁藥，或是單次非刻意誤觸。
3. 成果發表：Archives of Toxicology (2024) 98, 779–790

4. 榮獲獎項：113 年運動科學研究發展甲等獎勵
5. 申請國際計畫：延伸之研究題目申請美國公平競賽組織 Partnership for Clean Competition 研究補助，經審查構想書通過

【研究團隊】

**團隊成員：**張值維、洪紹鑫、田喬

**團隊簡介：**敝運動禁藥分析實驗室由張值維博士領導，專注於運動禁藥分析，運用層析與質譜技術進行醫藥相關研究。研究主題涵蓋替代生物檢體分析、非蓄意用藥風險評估，以及醫師與藥師的知識調查。

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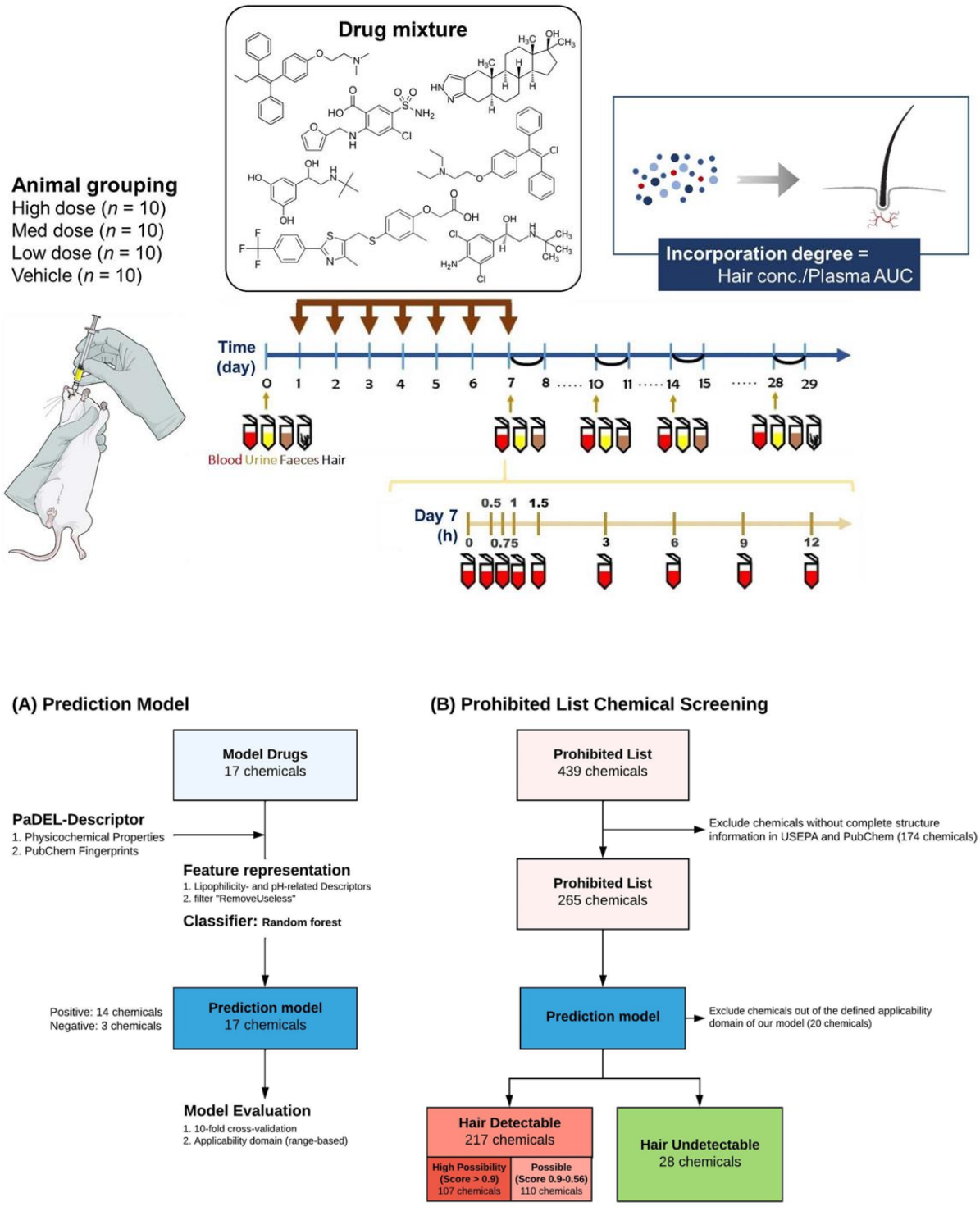
Hair analysis represents a significant methodology within the field of forensic toxicology, particularly with respect to its potential applications in elucidating the drug-use histories of athletes. Despite its prevalent application, the comprehension of the doping substances that can be detected in hair is still insufficient. This study aims to assess the viability of utilizing hair specimens for anti-doping purposes through a comprehensive and multifaceted approach.

An animal model was utilized to assess the dose-dependency and detection windows of 17 model drugs across various matrices. Using QSAR models, data regarding hair binding from animal studies were extrapolated to encompass all substances listed by the World Anti-Doping Agency. Additionally, a human study examining the consumption of diuretics and masking agents offered further validation of the findings.

Doping substances present in plasma exhibited the most pronounced dose dependency; however, they were characterized by limited detection windows. Urine and feces ranked next in terms of detection capabilities, while hair demonstrated the greatest retrospective capacity, with diuretics exhibiting the highest rates of binding to hair. It was predicted that most anabolic substances would be detectable in hair, whereas peptide hormones and $\beta$2-agonists were found to be undetectable, likely due to their substantial molecular weight and high polarity. A real-world study involving human hair, utilizing segmental analysis, corroborated the timing of administration for these diuretics.

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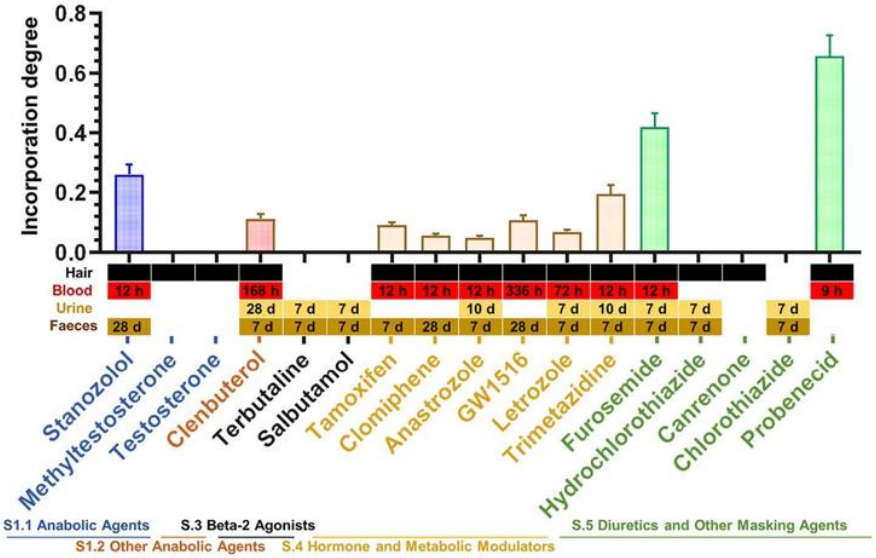


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【Concrete Results】

1. Through the analysis of segmented hair samples, even a minimal quantity of hair can provide insights into an athlete's drug use history over the course of an entire year, contingent upon the hair being of adequate length. Given that hair typically grows at a rate of approximately 1 cm per month, the timeline of drug exposure can be accurately determined.
2. Hair testing serves to ascertain whether an athlete has been involved in long-term intentional doping practices or has encountered a singular, unintentional exposure to prohibited substances.
3. Published Results: Archives of Toxicology (2024) 98, 779–790
4. Award Received: 2024 Class A Award for Excellence in Sports Science Research and Development.
5. International Project Application: A proposal for a follow-up study has been submitted for funding to the U.S.-based Partnership for Clean Competition and has successfully passed the concept review phase.

【Research Team】

**Team Members:** William Chih-Wei Chang, Shao-Hsin Hung, Ciao Tian

**Research Team Introduction:** The Anti-Doping Analysis Laboratory, under the direction of Dr. William Chang, specializes in anti-doping analysis and employs chromatography and mass spectrometry techniques for pharmaceutical research. The research areas encompass the analysis of alternative biological specimens, the assessment of unintentional medication risks, and surveys evaluating the knowledge of physicians and pharmacists regarding doping regulations.

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