Research progress of detection technology for illegal addition of prohibited substances in cosmetics

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Abstract. With the rapid development of the national economy and the vigorous development of China's cosmetics market, cosmetics have changed from a luxury product of skin care to a necessity, and its safety has increasingly become a concern of consumers. Hormones, preservatives, sunscreens and heavy metals in cosmetics are prohibited and restricted substances. The inspection of these prohibited and restricted substances is of great practical significance for enterprises to strictly control the product quality of cosmetics, ensure the safety of cosmetics and protect the health of the people. The incidents of illegal addition of banned substances in cosmetics emerge one after another, causing serious damage to the health of consumers and adverse effects on the domestic market. In order to provide technical support for relevant food and drug regulatory departments to find illegal additives in time and provide reference basis for Cosmetics testing, the author investigated and analyzed the possible prohibited components in cosmetics through collecting and inquiring relevant data of cosmetics and product investigation.

1. Status of illegal additives in cosmetics

In recent years, many cosmetic focus events have occurred in China, such as ‘chromium and neodymium’ events in cosmetics, asbestos problems in baby powder, 1,4-dioxane events in bath products, minoxidil detected in hair care products, phthalate events in perfume, m-phenylenediamine detected in hair dye, hydroquinone detected in whitening and freckle removing products, etc. The occurrence of these events or adverse reactions is mostly related to prohibited components in cosmetics.

A total of 1286 prohibited components (classes) are listed in China's Hygienic Standards for Cosmetics (2007). The national food and drug supervision and administration department has carried out cosmetic supervision and sampling inspection and risk monitoring throughout the country for many years. From the analysis of sampling inspection results in recent years, it can be seen that the quality and safety problems of cosmetics in China mainly include illegal addition, excessive amount of restricted substances, microbial pollution, etc., of which illegal addition is the most serious. The safety of cosmetics, especially the safety problems caused by the prohibited components of cosmetics, has received special attention from government regulatory departments, consumers and cosmetics related industries.
2. The type of illegal additives in cosmetics

According to relevant literatures [1-6], illegal addition of substances in powder, block defect, whitening, essence and wrinkles cosmetics is serious. All possible additives and adverse reactions are shown in Table 1.

| Category             | Possible additive                  | Adverse reaction                                                                                                                                                                                                 | Findings reported in the literature                                                                                     |
|----------------------|------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------|
| Powder cosmetics     | heavy metal[1]                      | Illegal addition of arsenic, cadmium, lead, mercury and other heavy metals beyond the standard, long-term contact with the skin, easy to increase skin sensitivity, resulting in "bloodiness", "skin cuticle thin" and other problems. Arsenic is highly toxic and can easily enter human cells, causing damage to internal organs. | Illegal excessive addition of arsenic, cadmium, lead, mercury and other heavy metals                                   |
| Concealer            | mineral substance[2]               | Antimony can be used as a material in alloys, paints, expectorants, semiconductors and so on. Although widely used, the toxicity is severe. Antimony poisoning can cause dermatitis, rhinitis, headache, vomiting and other symptoms | antimony                                                                                                               |
| Whitening cosmetics  | lead, mercury [3]                  | Lead poisoning can lead to acne and discoloration on the skin, and it can also affect the skin's metabolic rate. Excessive mercury can cause disorders of the body's physiological function system and damage the nervous system. | lead, mercury                                                                                                         |
| Synthetic perfume cosmetics | aldehydes, ketones and esters [3] | The essence does not have actual sense in the use process of cosmetic, a lot of synthetic essence have carcinogenic effect, overmuch use can affect central nervous system badly. | aldehydes, ketones and esters                                                                                         |
| "Quick effect" whitening cosmetics | glucocorticoid [4] | Long-term use contains the cosmetic of glucocorticoid to be able to cause the skin to become thin, blood capillary dilate, wool bursa atrophy, appear after bring about dry desquamate, couperose skin, hyperpigmentation phenomenon, once stop using hind can appear SAO urticant, red, papule wait for a symptom, cure very hard. | glucocorticoid                                                                                                         |
| Anti-wrinkle essence cosmetics | sex hormone [5]     | Long-term use of sex hormones may lead to pigmentation, dark spots, skin thinning, and even a high risk of cancer                                                                                             | sex hormone                                                                                                            |
| Acne cosmetics       | antibiotic [6]                     | Long-term exposure or ingestion of nitrofuran compounds may lead to cancer and teratogenicity baby.                                                                                                | furantoin, furazolidone, furantoin and furacillin                                                                   |
3. Detection technology of cosmetic prohibited substances

At present, there are the following methods for detecting various prohibited substances in cosmetics. These methods can effectively detect different components in cosmetics.

3.1. High performance liquid chromatography

Zhu [7] used for the determination of 22 kinds of dyes in hair dye by high performance liquid chromatography (HPLC). A DiscoveryRP-AmideC16 column (250mm×4.6mm,5μm) was used with acetonitrile-0.025mol/L phosphate buffer (pH6.0, containing 0.1% sodium heptanesulfonate ion pair reagent) as the mobile phase. The relative standard deviation (RSD) of the content of most of the components was less than 10%, and the recovery was 77.6% ≤ 122.8%.

Yang [8] established a high performance liquid chromatography (HPLC) method for the determination of carbamaric acid in whitening and freckle cosmetics. A C18 column was used. The eluent of 0.23% sodium lauryl sulfate solution and methanol (volume ratio 60≤40) was used as mobile phase for quantitative determination by high performance liquid chromatography (HPLC). The results showed that the linear relationship of carbamaric acid was good in the range of 0~1.073mg/mL, the detection limit was 1.45mg/g, and the average recovery was 104.36%.

Zeng [9] has established a high performance liquid chromatography (HPLC) method for the determination of isopropyl p-toluene sulfonate in cosmetics. Isopropyl p-toluene sulfonate was extracted with acetonitrile and centrifuged at high speed. The culture fluid was separated by 0.22 μm microporous filter membrane and separated by SuperLuC18 (250×4.6mm,5μm) column. The results show that under the optimized conditions, the linear range of isopropyl p-toluene sulfonate is 0.1~10 μg/mL, and the relative standard deviation of the method is 1.2% ≤ 2.1% in the range of 0.1~10 μg/mol. The results show that the relative standard deviation of isopropyl p-toluene sulfonate is 1.2% ≤ 2.1%.

Dou et al. [10] established a method for simultaneous determination of tetracycline hydrochloride and oxytetracycline dihydrate in cosmetics by high performance liquid chromatography-diode array detector (HPLC-PDA). A WatersSymmetryC18 (4.6mm×250 mm,5μm) column was used and the mobile phase was 0.01mol/L oxalic acid solution (pH=2.0)-acetonitrile-methanol with gradient elution. Results the linear range of the six components was 1 μg/ml ~ 100 μg/ml, the correlation coefficient was > 0.9995, the detection limit was 0.1 μg/ml, the recovery was 83.2% ≤ 107.9%. RSD was 0.5% ≤ 4.4% (n ≤ 6).

Wei [11] has established a relaxed high performance liquid chromatography (HPLC) method for the determination of fluorine in powdered cosmetics. The sample was extracted with saturated sodium chloride and ethyl acetate, purified by OasisHLB solid phase extraction column, separated by WatersBEHC18 column (2.1 mm×50 mm, 1.7 μm) and eluted with 0.1% acetic acid-acetonitrile-0.1% acetic acid aqueous solution as mobile phase gradient elution. Results there was a good linear relationship between the response value and the concentration of fluorine at 50ng/ml~500ng/ml. The detection limit of the method was 0.03 μ g / g, and the recovery of the samples was 82.4% ≤ 95.2% at three kinds of standard concentrations. The relative standard deviation (RSD) was 2.2% ≤ 4.6%.

3.2. Reversed-phase high performance liquid chromatography

Zhao et al. [12] established a reversed-phase high performance liquid chromatography (RP-HPLC) method for the determination of nine glucocorticoids, such as prednisolone and hydrocortisone, in cosmetics. Acidified methanol was extracted by oscillatory extraction, purified by HLB solid phase extraction column and separated and determined by HPLC. There is a good linear relationship between the response value and the concentration of fluoride at 50ng/ml~500ng/ml. The detection limit of the method was 0.03 μ g / g, and the recovery of the samples was 82.4% ≤ 95.2% at three kinds of standard concentrations. The relative standard deviation (RSD) was 2.2% ≤ 4.6%.

Zhao et al. [13] established a reversed-phase high performance liquid chromatography (RP-HPLC) method for the determination of seven banned colorants, such as alkaline purple and pigment red in cosmetics. After the sample was extracted with acetonitrile, a LunaC18 (150mm×2 mm, 5μm) column was used, acetonitrile and 4% ammonium acetate aqueous solution as mobile phase, gradient elution,
UV detection at 530nm wavelength. The detection limits of seven colorants ranged from 0.1 μg/mL, to 0.6 μg/mL. The recovery was 86.67% ≤ 98.67%, and the relative standard deviation was 4.11% ≤ 7.25%.

3.3. Ultra-high performance liquid chromatography
Wu [14] established an ultra-high performance liquid chromatography (UPLC) method for the determination of prednisone and cortisone in cosmetics. An ultra-high performance liquid chromatography (UPLC) with PDA detector was used. The chromatographic column was WatersAcquityUPLCTMHSST3C18 (100 mm×2.1 mm I.D., 1.8 μm). The mobile phase was acetonitrile aqueous solution and the gradient elution was carried out. The sample was extracted by methanol and detected by UPLC-PDA. The quantitative detection wavelength was 240 nm. Results: the recovery of the method was 88.3% ≤ 97.9%. The precision RSD was 1.4% ≤ 5.8%. When the linear range of concentration was 1.0 ~ 50.0 μg/mL, the regression coefficient of the working curve was $r ≥ 0.9991$.

Zhou [15] and other under the condition of methanol vortex ultrasonic extraction, established the simultaneous determination of hydrocortisone, triamcinolone acetonide acetate and chlorbetasol propionate in whitening and acne dispelling cosmetics. Ultra-high performance liquid chromatography (HPLC) of four glucocorticoids in Betamisone dipropionate. The chromatographic column was WatersACQUITYUPLCBEHC18 column (100 mm×2.1 mm, 1.7 μm). The mobile phase was acetonitrile-aqueous solution gradient eluting. The detection limits of the four corticosteroids were 0.03, 0.045, 0.075 and 0.075 ng, respectively. When the mass concentration was 1.040 mg/L, the correlation coefficient of the standard working curve was $r > 0.9998$, the recovery was 85.3% ≤ 102.8%, and the relative standard deviation was 2.1% ≤ 5.0% (n ≤ 6).

3.4. Atomic absorption spectrophotometry
Yan et al. [16] analyzed cosmetics samples A, B, C and D on the condition that the detection wavelength was 213.9 nm. Quantitatively determined MT in cosmetics by external standard method and discussed the condition of the method. Result: A method for the rapid determination of MT in food by atomic absorption spectrophotometer was developed, the method has good linear and reproducibility, the sample recovery was 92.4%~96.4%.

3.5. Thin-Layer chromatography
Wen [17] and others detected chloramphenicol in cosmetics with reference to the thin layer chromatography method in Chinese Pharmacopoeia 2000. Ethanol is used for extraction, silica gel GF254 prefabricated plate is used as a carrier, and chloroform-methanol (85:15) is used as a developing agent. The results showed that the minimum detection limit of the sample was 1.0 mg/g, and chloramphenicol was detected in 3 of 12 commercial cosmetics.

Li [18] et al. established a TLC method for the detection of illegal addition of hydroquinone and phenol in whitening and freckle-removing cosmetics. Taking various whitening and freckle removing cosmetics as samples, the sample solution was prepared by ultrasonic extraction. The developer was chloroform-acetone (7: 3), and the mixed solution of 10% potassium ferricyanide and 2% ferric chloride (1: 1) was used as the developer. Hydroquinone, phenol and methanol are added to prepare a solution with a certain concentration as a reference substance. The results showed that there were blue spots in the corresponding positions of the reference substance.

3.6. Gas chromatography
Liao [31] et al. established a gas chromatography method for the determination of ethyl hexyl glycerin in cosmetics. The cosmetics samples were extracted by methanol ultrasounds, Separation was performed by hp-5 (30m 0.32mm 0.25 m) capillary column, use the Flame Ionization detector (FID) to detection, use external standard method to quantitative analysis. Under the optimized experimental conditions, the linear relationship between the concentration of ethylhexylglycerol and the
concentration of glycerol in the range of 1~500mg/L was good, and the correlation coefficient was 0.9998. Sample addition test experiments were carried out at 3 concentration levels of 40mg/kg, 400mg/kg and 2000mg/kg, the average recovery was 97.3%~108.7%, the relative standard deviation was 0.9% ~ 5.1%, and the detection limit was 10mg/kg.

3.7. Rapid detection kit method
Fang [19] developed a rapid detection kit for mercury, hydroquinone and phenol in freckle-removing and whitening cosmetics. The rapid detection results were compared with the test data of laboratory instruments to analyze the feasibility, sensitivity and specificity of the kit in the field detection of health supervision.

3.8. Hyphenated detection techniques
The related methods are listed in Table 2.

| Analysis methods | References | Detecting substance |
|------------------|------------|---------------------|
| Gas chromatography-mass spectrometry (GC-MS) | Jin [20] | 21 common preservatives such as phenol and benzyl alcohol |
| Chen et al. [21] | Phenol and hydroquinone |
| Xu et al. [22] | Atranol and Chloroatranol |
| Liu et al. [23] | Minocycline hydrochloride, Oxytetracycline hydrochloride, Tetracycline hydrochloride, Chlortetracycline Hydrochloride, Doxycycline Hydrochloride, chloramphenicol, Metronidazole, lincomycin, clindamycin phosphate, prednisolone, prednisone, hydrocortisone, Cortisone, Methylprednisolone, Triamcinolone, Triamcinolone acetonide, Dexamethasone |
| Jin [24] | Acrylamide |
| Jian [25] | Lincolamide, tetracycline, nitrofuran antibiotics, chloramphenicol, metronidazole and other 20 prohibited substances (acne-eliminating cosmetics) |
| Inductively coupled plasma mass spectrometry (ICP-MS) | Wang et al. [26] | mercury |
| Ultra high performance liquid chromatography-tandem four-stage mass spectrometry (UPLC-MS/MS) | Hao [27] | Seven antibiotics (metronidazole, minocycline hydrochloride, dihydrotetracycline hydrochloride, tetracycline hydrochloride, chloramphenicol hydrochloride, doxycycline hydrochloride, chloramphenicol) (acne-eliminating cosmetics) |
| Liu et al. [28] | Six antibiotics (minocycline, oxytetracycline, tetracycline, aureomycin, doxycycline, chloramphenicol) and metronidazole |
4. Discussion

Illegal additives, like hazardous substance residues, have adverse effects on human health and need to be accurately detected through rapid detection methods [32, 33]. Thus, researches on related detection technology are not only applied to animal, agricultural products and food industries [34-39], water monitoring and antibiotics detection [40-42], medical physiological tests [43, 44], but also applied to chemical industry production.

In recent years, inspectors have done a lot of work in the detection of illegal additives in cosmetics. Through the investigation of "focus" events, supervision and sampling results, published quality investigation documents, product formulas and other information, we can understand the possible prohibited components in cosmetics [45]. However, the existing test methods are mainly based on the establishment of a target screening mode, and the applicability of the method is also to evaluate the target matrix sample, which has certain limitations [46]. The potentially dangerous banned substances contained in cosmetics will do great harm to human health. Only by accurately detecting toxic and harmful substances in cosmetics technically and prohibiting or restricting these prohibited ingredients in cosmetics at the level of standards and regulations can the safety of cosmetics be ensured. The exchange and sharing of data and information should be strengthened among various inspection agencies so as to effectively link up and complement the work of illegal cosmetic additive inspection. Jointly establishing and improving the inspection standards and inspection systems for illegal additives in cosmetics can provide technical support for cracking down on illegal additives in cosmetics, provide effective and accurate data for the cosmetics risk monitoring and early warning platform, lay a foundation for the establishment of China's cosmetics safety risk control system, and thus better safeguard the health rights and interests of consumers [47].

5. Conclusion

This article investigated and summarized the information of illegal additives in cosmetics and reviewed related testing methods, in order to provide reference and technical support for the national food and drug regulatory departments, and provide reference basis for the testing of illegal additives in cosmetics.

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