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VALIDATED ANALYTICAL METHODS FOR TRICLOSAN - AN ENDOCRINE DISRUPTOR LOADED IN PERSONAL CARE AND CONSUMER PRODUCTS: A REVIEW

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ABSTRACT

Triclosan (TCS) is a broad-spectrum antimicrobial agent that is frequently used in pharmaceuticals and in consumer as well as personal care products like toothpaste, soaps, detergents, toys and surgical cleaning process. Reports have shown that TCS is a potential endocrine disruptor. TCS causes antimicrobial resistance and also causes disrupted hormonal development. This review covers analytical methods carried out on TCS from a time period of 1994 to 2014, which includes 26 analytical methods comprising Spectrophotometric and Chromatographic methods like RP-HPLC, UPLC, LC-MS-MS and GC-MS methods were reported. Currently, TCS in loaded in most of the products we consume and due to its potential estrogenic and androgenic activity, analytical chemistry had played an essential role in quantifying the content of TCS present in pharmaceuticals and consumer products. The application of these methods and determination of TCS in various sources are also been discussed.

Keywords: Triclosan, Personal care products, Endocrine disruptor, Spectrophotometric and Chromatographic methods

1. INTRODUCTION:

TCS is effective against many different bacteria as well as some fungi and protozoa it is widely used as an antiseptic, preservative and disinfectant in healthcare and in many consumer products including cosmetics, household cleaning products, plastic materials, toys and paints. It is also included in surface of medical devices, plastic materials, textiles and kitchen utensils where it acts as a bactericide for extended periods of time. TCS causes antimicrobial resistance and also causes disrupted hormonal development. TCS has more prevalence in soaps, mouthwashes, shampoos, deodorants, toothpastes, cleaning supplies and pesticides **[1]**. Its IUPAC name is 5-Chloro-2-(2,4-diclorophenoxy) phenol **(Figure 1)**. At higher concentration it acts as a biocide with many cytoplasmic and membrane targets. At lower concentration it prevails in commercial products, it acts as bacteriostatic and it targets bacterial fatty acid synthesis **[2]**.

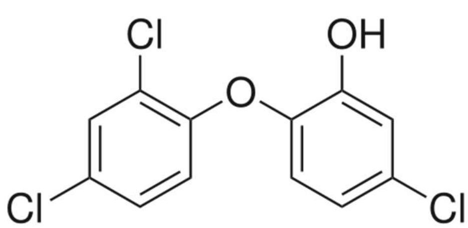

Figure 1: Structure of Triclosan

The chemical structure of TCS implies that its chemical properties are related to many toxic compounds such Polybrominated diphenyl ethers (PBDEs), Polychlorinated diphenyls (PCBs), Dioxins, Bisphenol A etc. **[3]**. Data from biological studies have demonstrated that TCS might have endocrine disrupting effects in humans and other animals **[4, 5]**. TCS exhibited estrogenic and androgenic activity in both ER- and AR-mediated bioassay **[6]**. TCS is also reported to have estrogenic activity as it can increase uterine weight in female rats **[7]**.

TCS traces are found in aquatic ecosystem and cannot be completely removed during waste water treatment process. It disrupts the Endocrine potential as antimicrobial in thyroid hormone haemostasis and also the reproductive axis. The use of TCS must be limited in places where it is highly effective **[8]**.

The potential for endocrine disruption and antibiotic cross-resistance highlights the importance of the judicious use of TCS, whereby the use of TCS should be limited to applications where it has been shown to be effective.

There are no review articles published emphasizing the importance of different analytical methods for the estimation of TCS in water samples, personal care and household products have be reported.

1.1. Appearance

Colourless, odourless, crystalline substance.

1.2. Solubility

Insoluble in water and soluble in 0.1N Sodium hydroxide **[9]**.

1.3. Applications

TCS is a broad spectrum antibacterial and antifungal agent in personal care products, industrial products and household products.

1.4. Mechanism of action

At higher concentration it acts as a biocide with many cytoplasmic and membrane targets. At lower concentration it prevails in commercial products, it acts as bacteriostatic and it targets bacterial fatty acid synthesis. It binds to the bacterial enoyl-acyl carrier protein reductase (ENR) enzyme. This binding increase the affinity of the enzyme NAD^+ that results in the formation of ENR-NAD^+-TCS complex which causes the bacterial inability to participate in fatty acid synthesis. These fatty acid are necessary for binding and reproducing cell membrane (WHO 2006).

1.5. Pharmacokinetics

After absorption, human metabolizes TCS by conjugation reaction in the Liver. It is being excreted via faeces and urine **[10]**.

1.6. Side-effects

Fever, allergies, endocrine disruption, hepatic problems, depression, cancer, antibacterial resistance.

2. ANALYTICAL METHODS FOR ESTIMATION OF TCS AND ITS COMBINATION

Development of new analytical methods were carried out, in order to quantify TCS individually or simultaneously in personal care and household products, to increase accuracy and sensitivity which includes Spectrophotometric **[11]** and Chromatographic methods like RP-HPLC **[12-20]**, UPLC **[21, 22]**, LC-MS-MS **[23-34]** and GC-MS **[35, 36]** methods. The developed methods were validated according to ICH guidelines in order to check the validation parameters such as linearity, range, Limit of Detection (LOD), Limit of Quantification (LOQ), accuracy, selectivity, sensitivity, robustness and ruggedness. The list of analytical methods for TCS was tabulated in **Table 1** and Proportion of analytical methods available for the estimation of TCS and its Combination is depicted in **Figure 2**.

Table 1: Analytical Methods for Estimation of TCS and its Combination

S. No.	COMPOUND	METHOD	SPECIFICATION	REFERENCES
1.	TCS	Cuvetteless UV–vis micro-spectrophotometry following simultaneous ultrasound assisted emulsification–microextraction with derivatization	Precision = 2% LOQ = 50 µg /g	11
2.	TCS TCC	HPLC SP:An Agilent SB-C18 anlytical column (250x4.6mm, 5µm) MP: methanol: phosphate(72:28V/V) Detection: UV at 280nm	Linearity = 0.110 µg/ml R^2: 0.999 Flow rate = 1.0mL/min	12
3.	TCC	Solid-Phase Extraction−LC with Stochastic Resonance Algorithm	LOD: 10-1ng/L LOQ: 50-5ng/L	13
4.	TCS TCC MTCS	Temperature-controlled ionic liquid dispersive liquid phase microextraction with ultra-HPLC	Linearity TCS, MTCS = 0.0100 - 100µg/L TCC = 0.00500 - 50.0µg/L $R^2 > 0.9903$ LOD = 1.15 - 5.33ng/g Recoveries Reclaimed water = 68.4% - 71.9% Irrigating water = 61.6% - 87.8% Waste water = 58.9% - 74.9% Dosmestic water = 64.9% - 92.4%	14
5.	TCS TCC	RP-HPLC SP:Devilosil RP Aqueos AR-5 RP-30 MP:Methanol:Water(90:10V/V) Flow rate:1.0mL/min Detection: DAD TSC=280nm TCC=265nm	Linearity: TCS = 0.5-20 $1^{-1/4}$g/mL TCC = 0.3-20 $1^{-1/4}$g/mL Retension time: TCS = 5.18min TCC = 8.13min Extraction efficiency: TCS = 97% TCC = 87% LOD: TSC = 0.04ng/mL TCC = 0.11 ng/mL LOQ: TCS = 0.17 ng/mL TCC = 0.50 ng/mL	15
6.	TCS	HPLC	Recovery: 7.5min Temperature: 40°C	16
7.	TCS TCC	Molecularly Imprinted Solid Phase Extraction Coupled with HPLC-UV SP:C_{18}SPE	LOQ: Soil sample TCS & TCC = 40µg/kg TCC = 100 µg/kg TCS = 300 µg/kg	17
8.	TCS	Ampherometric sensor based on electropolymerised MIP	Linearity: $2.0x10^{-7}$ to $3.0x10^{-6}$ mol/L LOD: $8.0x10^{-8}$ mol/L	18
9.	4 Fluoroquinolones Ofloxacin Norfloxacin Enofloxacin Levofloxacin	UA- DLLME with LC-UV	Linearity = 0.01- 2.0 µg/ml LOD = 0.14 - 0.81 µg/L Average recovery: 82.7 - 110.9% (with RSD less than 5.2% (n=3) Enrichment factors = 32 - 134 folds	19
10.	TCS TCC 4 transformation product in water samples	SPME-HPLC-DAD	MDL: Deionised sample = 0.06 - 0.21ng/ml River water sample = 0.12 - 0.73ng/ml Recoveries: Deionised sample = 84.62 - 100.80% River water sample = 81.54 - 102.32%	20
11.	Antimicrobial Preservatives BUVS's OPCs in fish.	UHPLC with tandem mass spectometry	Recovery : >70% Antimicrobial = 78.5 - 85.6% Preservatives = 85.0 - 89.4% BUVS's = 70.9 - 112% OPCs = 81.6 - 114% RSD = O.7 - 15.4% Repeatability = <19.8% & 19.0%	21

			LOD= 2 antimicrobials = 0.001 - 0.006ng/g 8 BUVS's = 0.0002 - 0.009ng/g 4 preservatives = 0.001 - 0.015ng/g 9 OPC's = 0.001 - 0.014ng/g	
12.	TCS TCC MTCS	DLLME with UHPLC-TUV	Linearity : TCS = 0.0500 - 100 µg/L TCC = 0.0250 - 5.0 µg/L MTCS = 0.500 - 100 µg/L R^2: >0.9945 LOD: 45.1 - 236 ng/L	22
13.	TCS TCC SEVEN PARABENS	LC/ESI-MS/MS	RECOVERY: >85% LOQ: 0.08-0.44ng/L Ubiquity: MeP & =1-6µg/Ln-PrP Coexistence=i-BuP & =100-200ng/L n-BuP	23
14.	TCC	SBSC-LD with LC-MS-MS	Precision = 2% LOQ = 10ng/g	24
15.	19 Compounds BADGES's BP-UV filters Parabens TCS TCC	LC-MS/MS	Matrix effect = +11 (2,3,4-trihydroxy benzophenone) to -86% (2,4-dihydroxy benzophenone) LOQ = 0.2-2.0 ng/mL Precesion: Ethyl paraben = 5.8% TCS= 24.0% Recovery : BADGES's = 25-135% BP-UV filters = 84-125% Parabens = 52-126% TCS = 75-118% TCC = 90-124%	25
16.	TCS	Microporous bamboo-activated charcoal solid-phase extraction combined with HPLC-ESI-MS	Linearity: 0.02-20µg/L R^2 > 0.9990 LOD = 0.002 µg/L Recovery: 97.6-112.5%	26
17.	12 acidic pharmaceuticals (NSAID's & bezafibrate)+2 aqueous metabolites+TCS		LOD: 6-200ng/L LOQ: 0.15-11ng/L	27
18.	TCS TCC	IL-DLPME prior to HPLC-ESI-MS-MS	Linearity : TCS=1-60 µg/ml TCC=0.2-12 µg/ml R^2: 0.9980 - 0.9990 LOD: 0.040 - 0.58 µg/ml Precision: 7.0-8.8% (RSD, n=5) Recovery: 70.0% - 103.5%	28
19.	TCS TCC	IDLC-tandem mass spectrometry	Recovery = 98.1% - 106.3% RSD = 1.8% & 18.1(n=6) LOQ TCS = 2.0µg/kg TCC = 0.2µg/kg	29
20.	TCS TCC	SPE with HPLC-ESI-MS"	Recovery: 89.5%-97.5% LOD: TCC = 1.0ng/L TCS = 2.5ng/L	30
21.	TCS TCC	IL-DLPME prior to HPLC-ESI-MS-MS	LOD: TCS = 0.5-100 µg/L TCC = 2.5-500 µg/L Repeatability: TCS = 6.4% TCC = 5.4% Recovery: 88% - 111%	31
22.	TCS TCC	TC-IL-DLME prior to HPLC-ESI-MS-MS	Linearity : TCS = 0.5-100 µg/L TCC = 0.1-20 µg/L R^2: 0.9990 LOD: TCS = 0.3 µg/L TCC = 0.04 µg/L Precesion (RSD, n=5)	32

			TCC = 4.7% TCS = 6.0%	
23.	TCS TCC Transformation product od TCC	SP-ME-HPLC-MS/MS	Recovery : Deionised sample = 97 - 107% River water sample = 99 - 110% LOD: Deionised sample = 0.32 - 3.44ng/L River water sample = 0.38 - 4.67ng/L	33
24.	TCS TCC	LC-MS-MS	Matrix effect (n=5) TCS=79.7+/-6.7 TCC=100.5+/-8.4% LOD: TCS=1.5ng/g (d.w), TCC=0.2 ng/g (d.w)	34
25.	TCS MTCS	Solid phase dispersion & GC-MS-MS	Recoveries: SEWAGW SLUDGE MTCS: 95.7 - 101.0% TCS: 97.4 - 101.3% SOIL SAMPLES MTCS: 98.4 - 101.0% TCS: 98.7 - 99.0% LOD: SEWAGW SLUDGE: 0.10 - 0.12ng/g SOIL SAMPLES: 0.05 - 0.08ng/g	35
26.	24 household HPV chemicals in municipal waste water system	LC&GC –MS/MS	Limits: 0.1-100ng/L (in water) Average recovery: 54 % - 112% (for most compounds)	36

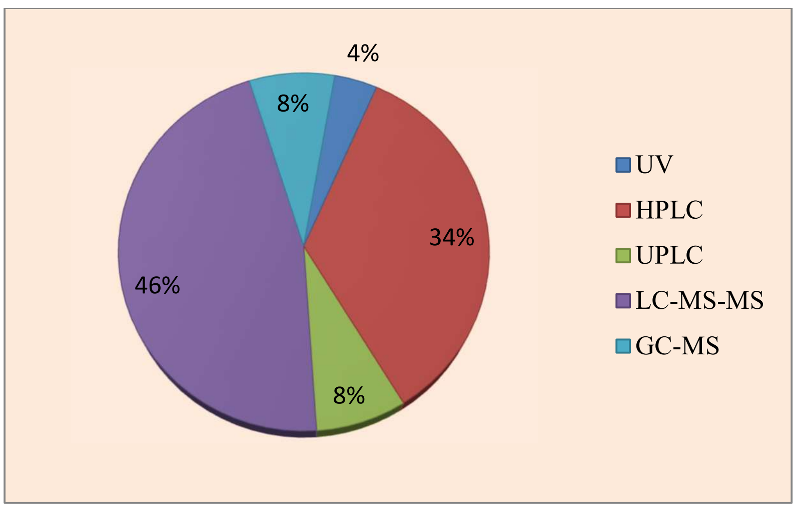

Figure 2: Proportion of analytical methods available for the estimation of TCS and its Combination

3. CONCLUSION

Several analytical methods like Spectrophotometric and Chromatographic methods like RP-HPLC, UPLC, LC-MS-MS and GC-MS methods have been developed for estimation of TCS individually, in combination and with their ingredients like Triclocarbon (TCC), Parabens etc., in water samples, personal care and household products have be carried out. The high importance of TCS is due to its action as antibacterial and antifungal agent promoted its use in various personal care and household products. On the other hand, keeping the toxic side effect of TCS as an endocrine disruptor on humans and other animals, the amount of TCS loaded in various products were quantified employing the developed and validated analytical methods. At the same time only few analytical methods including Spectrophotometric and Chromatographic methods has been reported. The reported Spectrophotometric method was less sensitive when compared to the Chromatographic methods which likely includes RP-HPLC, UPLC, LC-MS-MS and GC-MS methods, all these methods involves prior sample pre-treatment employing Solid phase extraction (SPE), which gave a good recovery of TCS from the samples on study. The developed Chromatographic methods were validated and they were found to be simple, sensitive and rapid. Due to the increased toxic concern of TCS, it is concluded that the proportion of analytical methods developed for TCS need to be increased in different typologies of samples, thereby the quantified amount creates an awareness to minimize the exposure to TCS to reduce the infertility rate in humans.

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