APPLICATION

TOC 9

TOC Analyses for Purified Water Water for Injection and Clean-In-Place Applications

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The changes to the US Pharmacopoeia monograph for the quality of purified water, water for injection, and cleaning water is under review and evaluation by the pharmaceutical industry. The current proposed method (1) will include the replacement of the oxidizable substances test by measuring total organic carbon (TOC).This test method will be used to evaluate the quality of Purified water and water for injection. The Pharmaceutical Research and Manufactures of America (PhRMA) has conducted the evaluation of several compounds (Table 1) to determine their performance as a system suitability standard. The validation of the 680°C TOC combustion technique for use in pharmaceutical and other ultra- pure applications is critical to ensure adequate recovery of the system suitability standard.

The primary concern to the pharmaceutical industry of the system suitability standard is the recovery of varying concentrations of compounds. These oxidizable substances typically should have a recovery of 85-115% of theoretical carbon concentration in the range of 0.25-10 PPM (2).When performing this type of application, utilizing the following parameters for the TOC-5000 series, the full capabilities of the modern 680° catalytically aided combustion technique can be achieved.

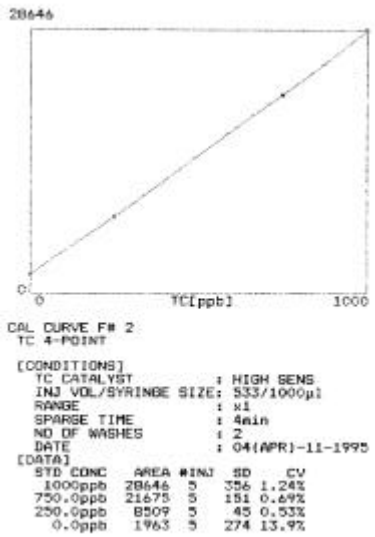

Fig. 1: Standard addition of KHP to pure reagent water

Instrumentation	
Shimadzu Instruments:	TOC 5000A with POC option and automatic sample injector ASI-5000A
Carrier gas:	Oxygene or synthetic air
Sparge temperatur:	RT
Sparge time:	4 min./pH 2-3

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The Shimadzu TOC-5000 series with the ASI-5000 series autosampler was utilized for all aqueous non-purgable organic carbon (NPOC) samples. Instrument setup was with high sensitivity catalyst-0.5% Pt, 1000ul syringe, sparge time-4 min.with automatic (ASI-5000) pH adjustment to pH 2-3 with 2.0 N HCl, minimum 3 injection per sample or standard, and 4 point calibration curves were developed using potassium hydrogen phthalate (KHP) as the organic carbon standard. A standard curve (Figure 1) was generated by the standard addition of KHP to pure reagent water (Rw)of 1000, 750, 250, and 0 ppb. Each compound analyzed was diluted to theoretical organic carbon concentrations of 750, 500, and 250 ppb. Three aliquotes of each dilution was analyzed. Each of the compounds' recoveries were calculated by the following :

$$\text{Recovery \%} = (([Cpd]_{TOC} - [Rw]) \div [Cpd]_{theoretical}) \times 100$$

Where:

$[Cpd]_{TOC}$ = the concentration of the diluted compound as measured on the TOC.
$[Rw]$ = the concentration of the diluent water as measred on the TOC.
$[Cpd]_{theoretical}$ = the theoretical carbon concentration of the compound.

Compound	Abreviated name	% Carbon
Sodium Dodecyl Sulfate	SDS	49.98
Sodium Dodecylbenzenesulfonate	SDBS	62.04
Nonoxynol	N-101	62.44
Octoxynol	X-100	60.68
Bovine Serum Albumine	BSA	46.67
Commercial glassware cleaner	Alconox	15.47
Sucrose	Sucrose	42.10
1,4-benzoquinone	Quinone	66.67
Naphthoresorcinol	Naph-OH	74.99
1-O-octyl-β-D-glucopyranoside	O-Gp	57.50

Table 1: Compounds Analyszed

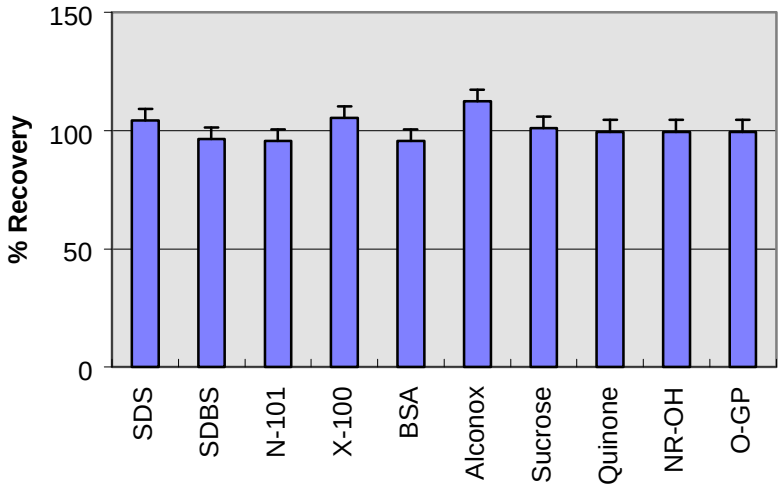

Fig. 2: Recovery of compounds tested

Conclusion

The TOC-5000 series utilizing the modern 680° C catalytically aided combustion technique meets or exceeds the parameters set for the percent recovery over a broad concentration range of any of the system suitability standards that were proposed by the PhRMA.

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