Titration Application Note

Iodimetric determination of Caffeine

Introduction

Caffeine is an alkaloid, belonging to class of methylxanthines and is widely used central nervous system (CNS) stimulant that reduces fatigue and drowsiness.

The most well-known sources for caffeine are the coffee beans, tea leaves and kola nuts. Caffeine is added to many popular soft drinks, and is also a component of a number of pharmacological preparations and over-the-counter medicines including analgesics, diet-aids, and cold/flu remedies. Along with its benefits, caffeine also has some negative effects on human system. Therefore, monitoring caffeine content in drinks or drugs is utmost important.

This application note describes the potentiometric determination of caffeine by iodometry using DMi140-SC combined platinum ring redox sensor.

Sample preparation and procedures

1. Titrant Preparation:
   Sodium thiosulfate c($Na_2S_2O_3$), 0.1 mol/L: Accurately weigh and dissolve 12.409 g of $Na_2S_2O_3.5H_2O$, in 200 mL deionized water and transfer it to a 500 mL volumetric flask then dilute up to the mark with deionized water.
2. Reagents:
   Iodine solution, ½ c(I_2), 0.1 mol/L:
   In a 1000 mL volumetric flask, dissolve 36 g of KI in 100 mL of deionized water. Dissolve 14 g of I_2 in the KI solution. Add 3 drops of conc. HCl and dilute up to the mark with deionized water. Store it in amber colored bottle to protect from light.
   0.1 mol/L H_2SO_4: Pipette out 2.720 mL from 98% Concentrated H_2SO_4 in a 500 mL volumetric flask containing 125 mL of deionized water. Adjust the final volume to 500 mL with deionized water.
3. Titer determination of $Na_2S_2O_3$, 0.1 mol/L:
   For details, refer to the application note M009.
4. Back Titration:
   Add 10 mL of deionized water to PP titration beaker.
   Add 20 mL of ½ I_2 solution and 10 mL of 0.1 mol/L H_2SO_4 to it.
   Filter this solution and titrate the filtrate against 0.1 mol/L $Na_2S_2O_3$.
   The back value is stored as B[Back value_Caff]
5. Sample Titration:
   Standard Caffeine Sample:
   Prepare a stock solution consisting of 4.85475 g weighed standard caffeine (Merck) and dilute up to the mark with deionized water in 500 mL volumetric flask.
   Pipette out 10 mL of this standard into a beaker.
   Add 20 mL of ½ I_2 0.1 mol/L and 10 mL of 0.1 mol/L H_2SO_4 solutions to the same beaker.
   Formation of brick-red colored precipitate takes place.
   Filter this precipitate and collect the filtrate into a PP titration beaker.
   Titrate the filtrate against 0.1 mol/L $Na_2S_2O_3$.

   Sample Preparation, pharmaceutical formulation containing 50 mg of caffeine per tablet:
   Take about 10 tablets, weigh them and grind them into fine homogeneous powder using mortar pestle. Store it in air tight container.
   Titration: Weigh the amount of powder that corresponds to 70 - 80 mg of caffeine in the sample into glass beaker.
   Add about 10 mL of deionized water to it, sonicate for 2-3 mins.

Add 20 mL of ½ I_2 0.1 mol/L and 10 mL of 0.1 mol/L H_2SO_4 solutions to the same beaker. Formation of brick-red colored precipitate takes place.
Filter this precipitate and collect the filtrate into a PP titration beaker.
Titrate this filtrate against 0.1 mol/L $Na_2S_2O_3$.

Chemistry

$C_8H_{10}N_4O_2 + 2\ I_2 + KI + H_2SO_4 \rightarrow$
$C_8H_{10}N_4O_2.HI.I_4 + KHSO_4$
$I_2 + 2Na_2S_2O_3 \rightarrow 2NaI + Na_2S_4O_6$

Solutions

- **Titrant**: Sodium thiosulfate, c($Na_2S_2O_3$) = 0.1 mol/L
- **Chemicals**:
  Iodine resublimed, I_2
  Concentrated H_2SO_4, 98%
  Concentrated HCl, 35%
  Potasssium iodide, KI
  Deionized water
- **Standard**:
  Potassium iodate, KIO_3, 20 - 30 mg
  Compound:
  Caffeine $C_8H_{10}N_4O_2$, M = 194.19, z = 4

Instruments and accessories

- Titration Excellence T5/T7/T9
- The method can be adapted on G10S/G20S titrators with slight modifications in the method.
- XP205 Analytical balance (11106027)
- DMi140-SC, combined platinum redox sensor (51109520)
- 2 - Burette DV1020 20 mL (51107502)
- Compact Stirrer (51109150)
- Titration beakers PP 100 mL (101974)
- Spatula
- LabX® software

Results

A. Titer Determination of $Na_2S_2O_3$ (as per M009)

Titer value obtained = 0.99609, n = 6
s = 0.000183; srel = 0.184 %

B. Content Determination of Caffeine in samples

	R2: Standard sample [%]	R2: Pharmaceutical sample [mg/tablet]
1	95.999	43.918
2	96.323	43.699
3	96.133	45.130
4	96.032	45.254
5	95.600	44.545
6	95.637	44.016
Mean	95.954	44.427
s	0.284	0.656
srel	0.296 %	1.476 %

The obtained results are systematically lower than expected, but the repeatability is good.

Remarks

The application method has been developed for the mentioned sample. It may be necessary to optimize the method for your sample.
It is necessary to perform back titration as excess iodine is titrated against $Na_2S_2O_3$.

On addition of I_2 and H_2SO_4, formation of brick red precipitate takes place due to reaction of caffeine and iodine. After filtration, the unreacted iodine is titrated with $Na_2S_2O_3$. If the titrating solution is taken without filtration, the reaction gets reversed where the precipitate solubilizes on $Na_2S_2O_3$ addition, resulting in to release of complete I_2 that was added in initial phase. Due to this the value obtained for titration is same as that of back titration. Therefore, during sample titration (standard / pharmaceutical), it is necessary to filter the sample and titrate the filtrate.

The sample factor used for calculation is the average weight of 10 tablets.
sf1= average weight of 10 tablets (0.8132 g).

Waste disposal and safety measures

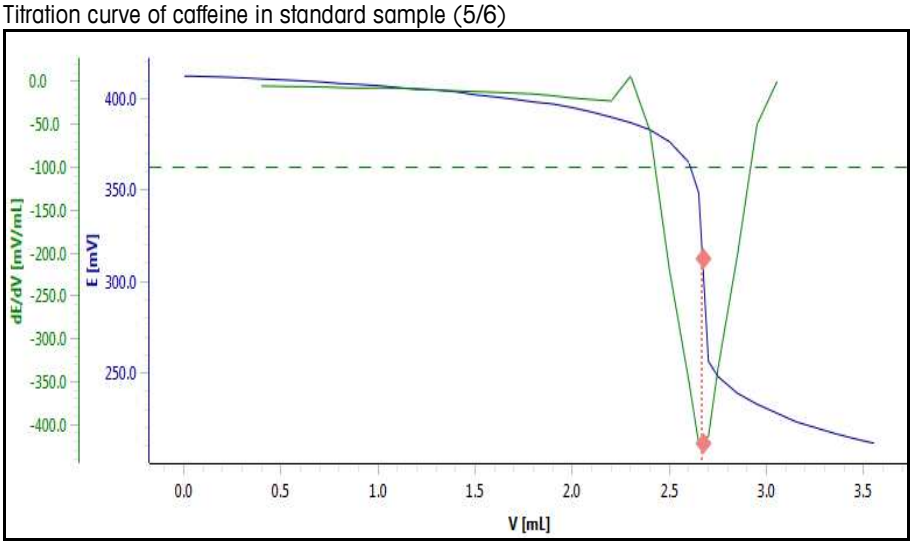
Dispose as aqueous waste.

Further information

http://www.mt.com/ch/en/home/products/Laboratory_Analytics_Browse/Product_Family_Browse_titrators_main/Titration_Excellence.html?cmp=als_Titration-Excellence

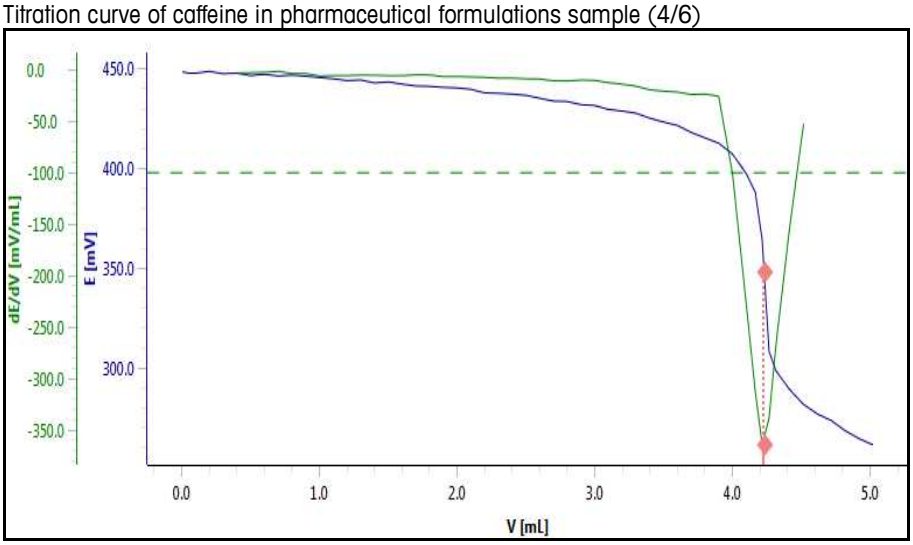
Measured values

Titration curve of caffeine in standard sample (5/6)



Volume [mL]	Measured Values [mV]	dE/dV [mV/mL]	Time [s]	EQP
0.000	412.2	NaN	0	
0.050	412.2	NaN	5	
0.100	412.0	NaN	10	
0.200	411.7	NaN	15	
0.300	411.3	NaN	20	
0.400	410.7	-5.20	25	
0.500	410.2	-5.71	30	
0.600	409.7	-5.98	36	
0.700	409.1	-6.25	41	
0.800	408.2	-7.13	46	
0.900	407.7	-7.69	51	
1.000	407.0	-7.40	56	
1.100	406.0	-7.76	61	
1.200	405.0	-8.55	66	
.....	.....	.....	.....	.....
2.200	389.8	-22.68	117	
2.300	386.8	6.25	122	
2.400	382.9	-57.58	127	
2.500	376.4	-219.52	132	
2.600	365.1	-349.37	137	
2.651	348.4	-421.89	142	
2.670465	312.5	-421.89	NaN	**EQP**
2.701	256.3	-413.83	158	
2.751	248.0	-333.73	164	
2.851	238.9	-201.51	171	
2.951	233.0	-50.29	176	
3.051	228.2	-1.66	182	
3.151	223.4	NaN	188	
3.251	220.2	NaN	193	
3.351	217.0	NaN	198	
3.451	214.2	NaN	203	
3.551	211.7	NaN	208	

Titration curve of caffeine in pharmaceutical formulations sample (4/6)



Volume [mL]	Measured Values [mV]	dE/dV [mV/mL]	Time [s]	EQP
0.000	448.6	NaN	0	
0.050	447.9	NaN	6	
0.100	447.9	NaN	11	
0.200	448.8	NaN	16	
0.300	447.6	NaN	21	
0.400	447.9	-3.04	27	
0.500	446.7	-2.87	32	
0.600	447.3	-2.47	37	
0.700	446.5	-1.54	42	
0.800	446.9	-3.58	48	
0.900	446.4	-3.66	53	
1.000	445.7	-6.04	58	
1.100	445.1	-5.61	63	
1.200	444.2	-5.64	68	
.....	.....	.....	.....	.....
3.500	423.4	-20.79	188	
3.600	421.7	-21.64	194	
3.700	418.2	-23.96	199	
3.800	415.5	-23.53	204	
3.900	412.8	-25.75	209	
4.000	407.4	-100.63	214	
4.100	397.6	-227.22	219	
4.166	388.2	-312.69	224	
4.216	364.3	-364.14	229	
4.230552	348.1	-364.23	NaN	EQP
4.266	308.5	-338.67	236	
4.316	298.7	-267.55	242	
4.416	289.2	-152.71	248	
4.516	281.9	-53.46	254	
4.616	277.1	NaN	259	
4.716	273.8	NaN	264	
4.816	268.8	NaN	270	
4.916	264.8	NaN	275	
5.016	261.7	NaN	280	

Method for caffeine in pharmaceutical sample

001 Title

Type	General titration
Compatible with	T5/T7/T9
ID	—
Title	Assay of caffeine: Sample titration

002 Sample

Number of IDs	1
ID 1	—
Entry type	Weight
Lower limit	0.0 g
Upper limit	2.0 g
Density	1.0 g/mL
Correction factor	1.0
Temperature	25.0°C
Entry	Arbitrary
Titrator	None
Number of sample factors	1
Name of sample factor	Avg Wt of tablet
Value of sample factor	0.8192

003 Titration stand (Manual stand)

Type	Manual stand
Titration stand	Manual stand 1

004 Stir

Speed	45 %
Duration	60 s
Condition	No

005 Titration (EQP) [1]

Titrant	
Titrant	$Na_2S_2O_3$
Concentration	0.1 mol/L
Sensor	
Type	mV
Sensor	DMi140-SC
Unit	mV
Temperature acquisition	
Temperature measurement	No
Stir	
Speed	45 %
Predispense	
Mode	None
Wait time	0 s
Control	
Control	User
Titrant addition	Dynamic
dE (set value)	8 mV
dV (min)	0.05 mL
dV (max)	0.1 mL
Mode	Equilibrium controlled
dE	1 mV
dt	2 s
t (min)	5 s
t (max)	30 s
Evaluation and recognition	
Procedure	Standard
Threshold	100
Tendency	None
Ranges	0
Add. EQP criteria	Steepest jump
Steepest jumps	1
Termination	
At Vmax	10 mL
At potential	No
At slope	No
After number of recognized EQPs	Yes
Number of EQPs	1
Combined termination criteria	No
Accompanying Stating	
Accompanying stating	No
Condition	
Condition	No

006 Calculation R1

Result	Content
Result unit	mg/tablet
Formula	R1 = (B[Back value_Caff]-Q)*C*sf1/m
Constant	C = M/z
M	M[Caffeine]
z	z[Caffeine]
Decimal places	3
Result limits	No
Record statistics	Yes
Extra statistical func.	No
Send to buffer	No
Write to Smart Tag	None
Condition	No

007 End of sample

008 Record

Summary	No
Results	Per sample
Raw results	Per sample
Table of meas. Values	Yes
Sample data	No
Resource data	No
E – V	Yes
dE/dV – V	Yes
log dE/dV –V	No
d2E/dV2 – V	No
BETA – V	No
E – t	No
V – t	No
dV/dt – t	No
T - t	No
E – V & dE/dV – V	Yes
V – t & dV/dt – t	No
Method	No
Series data	No
Condition	No

Method for Back value of Caffeine

001 Title

Type	General titration
Compatible with	T5/T7/T9
ID	—
Title	Assay of caffeine: Back value titration

002 Sample

Number of IDs	1
ID 1	Back value Caff
Entry type	Fixed volume
Volume	10 mL
Density	1.0 g/mL
Correction factor	1.0
Temperature	25.0°C
Entry	Arbitrary
Titrator	None
Number of sample factors	0

003 Titration stand (Manual stand)

Type	Manual stand
Titration stand	Manual stand 1

004 Stir

Speed	45 %
Duration	60 s
Condition	No

005 Titration (EQP) [1]

Titrant	
Titrant	$Na_2S_2O_3$
Concentration	0.1 mol/L
Sensor	
Type	mV
Sensor	DMi140-SC
Unit	mV
Temperature acquisition	
Temperature measurement	No
Stir	
Speed	45 %
Predispense	
Mode	None
Wait time	0 s
Control	
Control	User
Titrant addition	Dynamic
dE (set value)	8 mV
dV (min)	0.05 mL
dV (max)	0.1 mL
Mode	Equilibrium controlled
dE	1.0 mV
dt	2 s
t (min)	5 s
t (max)	30 s
Evaluation and recognition	
Procedure	Standard
Threshold	100
Tendency	None
Ranges	0
Add. EQP criteria	Steepest jump
Steepest jumps	1
Termination	
At Vmax	25 mL
At potential	No
At slope	No
After number of recognized EQPs	Yes
Number of EQPs	1
Combined termination criteria	No
Accompanying Stating	
Accompanying stating	No
Condition	
Condition	No

006 Calculation R1

Result	Back value Caff
Result unit	mmol
Formula	R1 = Q
Constant	C = 1
M	M[None]
z	z[None]
Decimal places	5
Result limits	No
Extra statistical func.	No
Send to buffer	No
Write to Smart Tag	None
Condition	No

007 End of sample

008 Blank

Name	Back value Caff
Value	B = Mean [R1]
Unit	mmol
Limits	No
Condition	No

009 Back value Caff

Result	Back value Caff
Result unit	mmol
Formula	R2 = Mean [R1]
Constant	C = 1
M	M[None]
z	z[None]
Decimal places	5
Result limits	No
Send to buffer	No
Condition	No

0010 Record

Summary	No
Results	Per sample
Raw results	Per sample
Table of meas. Values	Yes
Sample data	No
Resource data	No
E – V	Yes
dE/dV – V	Yes
log dE/dV –V	No
d2E/dV2 – V	No
BETA – V	No
E – t	No
V – t	No
dV/dt – t	No
T - t	No
E – V & dE/dV – V	Yes
V – t & dV/dt – t	No
Method	No
Series data	No
Condition	No