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COMMUNICATIONS

QUANTITATION OF INK TRANSFERRED DURING PHARMACEUTICAL PRINTING OPERATIONS USING INDUCTIVELY COUPLED PLASMA ATOMIC EMISSION SPECTROSCOPY

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ABSTRACT

The identification of solid dosage forms is often achieved through printing with a non-toxic ink. Due to product purity requirements, a method to quantify the amount of ink applied to tablets and capsules is of interest to the pharmaceutical industry.

The following presentation investigated the use of inductively coupled plasma atomic emission spectroscopy (ICP-AES) as a direct method of quantifying the amount of ink on a tablet. Because the ink used contained an iron oxide pigment of known composition, quantitation of the iron content could be used to measure the amount of ink transferred to the tablet.

The quantitative results obtained using ICP-AES were in agreement with calculated values for the volume of ink in the gravure roll. Tablets exposed to "double printing" were easily detected by the ICP-AES method.

INTRODUCTION

The following study was conducted to determine the amount of ink which is transferred to a pharmaceutical dosage form during the printing process. The determination of the amount of ink is complicated by the printing process, because ink can be lost in a number of ways as it is transferred to the substrate. During the printing process, ink is transferred into the logo cavity engraved into the metal design roll as it passes through the ink pan. A blade scrapes the excess ink from the surface of the design roll and uniformly fills the cavity. The ink is

transferred to a rubber roll, which applies the logo to the surface of the tablet. Incomplete transfer of the ink occurs at each of the steps in this process.

Inductively coupled plasma atomic emission spectroscopy (ICP-AES) was used to quantitate the amount of ink transferred to printed tablets. This method, which is based on the ability of ICP-AES to quantitate trace metals, is suitable for the analysis because the colorant in the ink is an iron oxide pigment. Determining the amount of iron present thus gave a direct measure of the amount of ink transferred to the tablet. From the dimensions of the logo cavity, and the density of the ink, the theoretical maximum amount of ink that could be transferred was calculated so that the efficiency of ink transfer during the printing operation could be determined.

METHODS

Manufacture of Printed Tablets

Placebo tablets were compressed and film coated (white) with an aqueous based dispersion of hydroxypropylmethyl cellulose and plasticizer.[1] The coated tablets were printed with an aqueous based ink[2] with "Glaxo" on one side and a 3 digit identification code on the opposite face using a double gravure offset printer.[3]

Quantitation of Ink Using ICP-AES

The printed portion of the tablet was scraped with a carbon steel blade, ensuring that all of the print was removed. The scrapings were weighed and placed into a microwave digestion vessel. An unprinted portion of the same tablet was scraped (to obtain approximately the same weight of shavings) and placed into a separate microwave digestion vessel as a control sample to allow background correction. Five mL of either 0.5 or 5.0% v/v nitric acid were added to each vessel which was then sealed and digested for a sufficient time in the microwave to achieve a pressure of 70 psi for approximately 3-5 minutes. [Either concentration of nitric acid may be used. The percent was increased to 5.0% because this concentration gave better reproducibility to the measurements.] After cooling, 250 µL of concentrated hydroflouric acid was added to each vessel and the

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1. Opadry®, Colorcon, West Point, PA.

2. Opacode WB®, Colorcon, West Point, PA.

3. Delta Printer, R.W. Hartnett Company, Philadelphia, PA.

sample was further digested for sufficient time in the microwave to achieve a pressure of 70 psi for approximately 3-5 minutes. The solution was centrifuged for approximately 10 minutes at 4000 RPM and then filtered through a 0.45 µm PTFE filter prior to analysis. Fourteen samples and 14 controls (from 14 different tablets) were prepared.

A spiked sample was prepared in the same manner as the samples in the previous section. An unprinted tablet was scraped to obtain approximately the same average weight as the samples in the previous section. After the addition of the digestion solvents, 200 µL of the 10 ppm iron standard was spiked into the digestion vessel. The spiked sample was then digested and analyzed with the samples prepared in the previous section.

The samples were analyzed in triplicate by ICP-AES using the parameters listed in Table 1. The amount of ink present was calculated using Equation 1.

$$\text{µg ink/tablet} = \frac{\{(A_s \times V_s) - [(A_b \times V_b \times W_s)/W_b]\} \times P_1}{P_2} \qquad \text{(Equation 1)}$$

where:

A_s = µg/mL iron in the sample
V_s = volume of the sample (5.25 mL)
A_b = average µg/L iron in the sample blanks
V_b = volume of the sample blank (5.25 mL)
W_s = weight of sample scraping (µg)
W_b = average weight of blank scrapings (µg)
P_1 = percent of solids in the ink (39%)
P_2 = percent of iron in the ink (17%)

Determination of the Theoretical Amount of Ink Transferred to the Tablets

The maximum amount of ink which could be theoretically transferred to the tablet was determined by calculating the area of the logos on the design roll using a gravimetric method. This area was then multiplied by the depth of the cut into the design roll to determine the volume of ink contained in the cavity.

The area of the printed logo was determined by photocopying each of the individual symbols and weighing the copy of the logo. To improve the accuracy of the measurement, a proof of

TABLE 1

Parameters for ICP-AES Analysis

Instrument:	Jobin-Yvon JY 38 Plus ICP
Wavelength	238.208 nm
Plasma Power:	900 Watts
Viewing Height:	12 mm above load coils
Entrance Slit:	30 µm
Exit Slit:	35 µm
Nebulizer:	Meinhard (glass concentric) Type C
Nebulizer Gas:	Argon at 2.95 bar
Nebulizer Gas Flow:	1.2 mL/min
Nebulizer Uptake Rate:	1.0 mL/min
Spray Chamber:	Scott type glass
Purge Gas:	Nitrogen at 4 L/min
Coolant Gas Flow:	14 L/min
Sheath Gas Flow:	0.2 mL/min
Standards:	10 mg/mL iron in 0.5% or 5.0% v/v nitric acid 0.5% or 5.0% v/v nitric acid

the logo (drawn to the same scale as the actual tablet printing) was successively enlarged on a commercial photocopier[4] until the symbols were expanded in area by a factor of 1024. The expanded symbols were traced onto paper of uniform consistency, and the symbols cut along their edges and weighed. A calibration curve was produced by weighing pieces of the same

4. Kodak Ektaprint 90 Copier, Eastman-Kodak, Rochester, NY.

paper that were of known areas. The area of the logo was then determined by comparison to the calibration curve generated from the pieces of paper of known area.

Equation 2 was used to calculate the theoretical amount of solids from the ink deposited onto the tablet surface.

$$\text{Amount of Solids } (\mu g) = A \times D \times \rho \times P \times 10^6 \qquad \text{(Equation 2)}$$

where:

A = logo area = 0.0378 cm^2
D = depth of embossment = 22 µm or 2.2×10^{-3} cm
ρ = specific gravity of ink = 1.2 g/cm^3
P = percentage of solids in ink expressed as a decimal = 0.39
10^6 = factor to convert from g to µg

RESULTS AND DISCUSSION

Table 2 summarizes the analytical results obtained for the amount of ink printed on each tablet using ICP-AES. With the exception of Tablet #5, the results are all of the same order of magnitude (range 16.1 - 26.6 µg). Tablet #5 contains approximately twice the amount of ink as the others. This discrepancy can be attributed directly to the printing process. Occasionally, one of the links carrying the tablets through the rubber printing rolls is not filled. As a result, this position on the roll does not discharge ink onto a substrate during that printing cycle. The rubber roll then receives a second quantity of ink from the metal gravure roll during the next cycle. The additional ink is then transferred to the next tablet when it comes in contact with the rubber roll. The print on such tablets is bolder.

The average amount of ink transferred to a tablet (excluding Tablet #5) was 22 µg, with a relative standard deviation (RSD) of 17.8%. The RSD demonstrates considerable variability in the amount of ink deposited. Some tablets had incomplete printing, with the top or bottom portions of the print cut off. The observed variability could also be attributed to the precision of sample preparation, which may be dependent on the quantity of core excipients which are scraped into the sample. However, the precision of the analytical method is demonstrated by the low RSD (3.4%) for replicate readings of a single tablet sample, and by the excellent spike recovery of 100.2% of the expected value. Table 3 contains the maximum theoretical quantity of ink which can be transferred to a tablet during the printing process,

TABLE 2

AVERAGE VALUES FOR AMOUNT OF INK (DRY SOLIDS) TRANSFERRED TO TABLETS DETERMINED BY ICP-AES

Sample	Amount of Dry Ink (µg)	Sample	Amount of Dry Ink (µg)
1	20.1	9	18.5
2	25.7	10	21.8
3	26.6	11	21.2
4	26.3	12	17.0
5*	49.5	13	16.5
6	25.2	14	20.9
7	25.0	Average	22
8	16.1	RSD	17.8%

*Value not used in calculation of average and RSD.

TABLE 3

THEORETICAL MAXIMUM AMOUNT OF INK (DRY SOLIDS) TRANSFERRED TO TABLETS DETERMINED GRAVIMETRICALLY

Sample	Area of Engravings (cm^2)	Amount of Dry Ink (µg)
1	0.0368	37.9
2	0.0383	39.4
3	0.0383	39.4
4	0.0381	39.2
5	0.0374	38.5
Average		39
RSD		1.7%

based on the gravimetric calculations. The reported value is the average of five replicate samples, which provided an estimate of the error of the quantitative method. The maximum quantity of dry solids transferred to the tablet surface during printing was determined to be 39 µg.

In calculating this value, several assumptions pertaining to ink transfer and the dimensions of the cavity of the design roll were made. The first assumption was that the shape of the design roll cavity was rectangular. In reality, the bottom corners of the actual engravement are rounded, and the calculated volumes were therefore slightly higher than the true values. The second assumption was that all of the ink contained in the cavity of the design roll was transferred to the rubber roll during the printing process. The ink transfer was actually incomplete due to interfacial tension between the ink and metal surface of the design roll, resulting in a residual quantity being retained in the logo cavity. The final assumption was that once on the rubber roll, the ink was completely transferred to the tablet surface. In reality, some residual ink remains on the rubber roll following transfer.

The efficiency of ink transfer during the printing process was determined from the ratio of the actual and theoretical amount of ink transferred. Using the results obtained by the ICP-AES and gravimetric experiments, 56% of the ink in the design roll cavity was deposited onto the surface of the tablet. The efficiency value reported is specific for the conditions used to print the particular tablets examined in this experiment. The percentage of ink transferred is dependent on such factors as the dimensions of the design roll embossment, elasticity of the rubber rolls, ink viscosity (and other properties of the ink which can affect its surface tension), and printer set up conditions.

CONCLUSIONS

ICP-AES was demonstrated to be an accurate method to quantitate the amount of ink transferred to a tablet substrate during the printing process. The calculated value for the amount of ink transferred during tablet printing using ICP-AES was 22 µg (RSD = 17.8%), compared to a theoretical quantity of 39 µg (RSD = 1.7%) determined through gravimetric analysis. A comparison of the values indicates a 56% efficiency of ink transfer from the gravure roll to the the tablet surface during the printing operation. Reported values are specific for this experimental set-up and could vary for alternate printing processes.

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