Malaysian Journal of Pharmaceutical Sciences,
Vol. 3, No. 2, 31–41 (2005)

STABILITY AND COMPATIBILITY OF TAXOL WITH VARIOUS DRUGS DURING SIMULATED Y-SITE ADMINISTRATION

JIN PIL BURM*
280 Seoseok Dong, Dong Ku, Kwangju, 501-140, Korea
Chosun Nursing College

This study evaluates the compatibility and stability of Taxol with ondansetron, ranitidine, vancomycin and cephalosporins in 5% dextrose injection and 0.9% sodium chloride injection during simulated Y-site administration. Two stock solutions of Taxol 0.3 and 1.2 mg/mL and each stock solutions of ondansetron 0.03, 0.1 and 0.3 mg/mL, ranitidine 0.5 and 2 mg/mL, vancomycin 1, 5 and 10 mg/mL and cephalosporins 20 mg/mL were prepared in glass bottles. Two mL of Taxol stock solution was mixed with 2 mL of each stock solution. Samples were removed at room temperature at time zero, one, two, four and 12 hours for immediate assay. Taxol concentrations were analyzed by High Performance Liquid Chromatography. All solutions were prepared in triplicate, and each drug was assayed in duplicate. At the time of sampling assay and before any dilution, each sample was visually inspected for clarity, color and precipitation. The pH was also determined. Taxol in concentrations of 0.3 and 1.2 mg/mL was stable when mixed with either ondansetron (0.03, 0.1 or 0.3 mg/mL, as the hydrochloride salt), ranitidine (0.5 or 2.0 mg/mL, as the hydrochloride salt), vancomycin (1, 5 or 10 mg/mL, as the hydrochloride salt) or cephalosporins 20 mg/mL and stored in glass containers for 12 hours. No precipitates, color changes, or haziness was seen. The changes in pH were minor.

Keywords: *Stability, Taxol, Ondansetron, Ranitidine, Vancomycin, Cephalosporins*

INTRODUCTION

Severely-ill patients often require extensive multiple intravenous drug therapy during their treatment; those in intensive care may receive as many as 20 medications (Gundlach *et al.* 1991) making management of i.v. administration and access a challenge. Taxol (paclitaxel) is one of the most active new agents introduced into cancer therapy (Wall and Wani 1977). The drug is most commonly administered as a continuous infusion over 12 hours every three weeks. Patients treated with Taxol may receive various drugs to treat nausea, vomiting, peptic ulcer and infection associated with antineoplastic therapy.

In clinical trials, the drug should be prepared in glass bottles and administered through tubing of material other than polyvinylchloride

* Corresponding author: Jin Pil Burm, e-mail: jpburm@venus.cnc.ac.kr

(PVC) because the plasticizer, diethylhexyl phthalate, has been shown to be extracted from the PVC tubing and containers (Rowinsky *et al.* 1990; Venkataramanan *et al.* 1981). With the recent Food and Drug Administration (FDA) approval of Taxol for the treatment of ovarian cancer (Donehower *et al.* 1987), many questions concerning the compatibility and stability of Taxol in a variety of containers and with various drugs need to be addressed. Waugh *et al.* (1991) reported on the stability, compatibility and plasticizer extraction of Taxol when the drug was diluted by various solutions and stored in various containers. Trissel and Bready (1992), and Trissel and Martinez (1993) reported turbidimetric assessment of the stability of Taxol when the drug was mixed with other drugs. Burm *et al.* (1994) reported the stability of Taxol in the presence of fluconazole, during simulated Y-site administration. Trisssel *et al.* (1998) and Zhang *et al.* (1997) reported compatibility and stability of Taxol combined with doxorubicin or with cisplatin and with carboplatin in infusion solutions. The unique formulation used to solubilize Taxol has led to an increased awareness of plasticizer-leaching issues, Taxol stability in solution, and Taxol compatibility with other medications. Particularly with longer Taxol infusion schedules, both drug stability in solution and pump apparatus congruence require careful consideration to minimize plasticizer-leaching problems and to ensure optimum drug delivery (Boyle and Goldspiel 1998; Sautou-Miranda *et al.* 1999).

Despite knowledge of the physical compatibility of Taxol with numerous drugs, a paucity of research has documented the specifics of Taxol's chemical compatibility with other medications. Thus, the purpose of this study is to evaluate the compatibility and stability of Taxol with ondansetron, ranitidine, vancomycin and cephalosporins in 5% dextrose injection and 0.9% sodium chloride injection during simulated Y-site administration at clinically relevant concentrations.

METHODS

Materials

Taxol was kindly provided by Bristol-Myers Squibb Co. Ondansetron (as the hydrochloride salt) and ranitidine (as the hydrochloride salt) were kindly provided by Glaxo Inc. Vancomycin (as the hydrochloride salt) was kindly provided by Lilly Co., ceftezole sodium and cephradine (first-generation cephalosporins) were kindly provided by Shinpoong Co.,

cefamandole sodium and cefmetazole sodium (second-generation cephalosporins) were kindly provided by Daewoo and Daewoong Co., cefoperazone sodium and cefotaxime sodium (third-generation cephalosporins) were kindly provided by Daehwa and Kukje Co., and cefepime hydrochloride (fourth-generation cephalosporin) was kindly provided by Boryung Co. Five percent dextrose injection and 0.9% sodium chloride injection were purchased from Choongwae Co. All other chemicals were reagent grade.

Preparation of solutions

Two stock solutions of Taxol 0.3 mg/mL and 1.2 mg/mL were prepared by diluting 2.5 and 10 mL of 6 mg/ml Taxol by using pipett, respectively, to 50 mL of 5% dextrose injection and 0.9% sodium chloride injection in glass bottles. Three stock solutions of ondansetron 0.03, 0.1 and 0.3 mg/mL were prepared by diluting 0.75, 2.5 and 7.5 mL of 2mg/mL ondansetron, respectively, to 50 mL of 5% dextrose in water and 0.9% sodium chloride injection. Two stock solutions of ranitidine 0.5 and 2 mg/mL were prepared by diluting 1 and 4 mL of 25 mg/mL of ranitidine, respectively, to 50 mL of 5% dextrose in water and 0.9% sodium chloride injection. Three stock solutions of vancomycin 1, 5 and 10 mg/mL were prepared by diluting 500 mg vial of vancomycin, respectively, to 500, 100 and 50 mL of 5% dextrose injection and 0.9% sodium chloride injection. One stock solution of cephalosporins 20 mg/mL were prepared by diluting 1 g vial of cephalosporins, respectively, to 50 mL of 5% dextrose injection and 0.9% sodium chloride injection in glass bottles.

Allen and Stiles (1981), and Allen *et al.* (1977) demonstrated that secondary admixtures injected through a Y-injection port, mix with the primary i.v. fluid in a 1:1 ratio. To simulate this condition for low and high concentrations of Taxol, 2 mL of Taxol stock solution was mixed with 2 mL of each stock solution. Separate admixtures were prepared for the assay of Taxol. Samples were removed at room temperature at time zero, one, two, four and 12 hours for immediate assay. All solutions were prepared in triplicate, and each drug was assayed in duplicate. At the time of sampling assay and before any dilution, each sample was visually inspected for clarity, color and precipitation. The pH was also determined.

High-performance liquid chromatographic assays

The Taxol HPLC assay was modified from the method reported before by Burm *et al.* (1994). The mobile phase consisted of acetonitrile:12.5 mM ammonium phosphate (60:40 v/v). The pH was adjusted to 4.5 with 1 N hydrochloric acid. The mobile phase was filtered through a Sartorius 0.45 micrometer nylon filter and degassed under vacuum in an ultrasonic bath. A Hitachi Intelligent Pump delivered the mobile phase at a flow rate of 1 mL/min appropriate for Taxol analysis. The column used for Taxol was an adsorbosphere C_{18} column (5 µm, 250 × 46 mm ID). A Hitachi UV-VIS Detector was set at a wavelength of 227 nm. Injections were made using a Hitachi autosampler. Taxol 1.2 mg/mL samples were diluted 1:4 and 20 µℓ of the resulting solution injected. Chromatographic data were recorded on a Hitachi Chromato-Integrator and the peak area was used for quantification. The various concentrations were determined by comparing the peak area with the standard curve. A standard curve was determined daily using five standard concentrations. In addition, a quality control sample and blank 5% dextrose injection and 0.9% sodium chloride injection were run daily. The standard curves had ranges of 40–200 µg/mL (200, 150, 100, 60 and 40 µg/mL) for Taxol. Taxol standard solutions were made by dissolving Taxol in methanol and diluting them with 60% acetonitrile. All solutions were kept refrigerated at –4°C when not in use to avoid evaporation of the organic solvent. Standard curves in the linear analytical concentration range for each drug were constructed for calibration. The correlation coefficient of each curve was higher than 0.999. Detection limit was defined below 100 ng/mL and the intraday and interday coefficients of variation were < 4% for each of the standard solutions.

Validation of assay

The chromatographic measurement of Taxol was established by chromatographic separation of Taxol from its preservatives (Cremophor and dehydrated alcohol) from various drugs. The stability indicating nature of the assays was established by forcible degradation of the Taxol 200 µg/mL and various drugs solutions. Samples were exposed to 1 N sodium hydroxide or 1 N hydrochloric acid for five hours at 60°C, 3% hydrogen peroxide for 12 hours at room temperature. All degradation products of Taxol and various drugs did not interfere with the intact drug in the assay (Fig. 1).

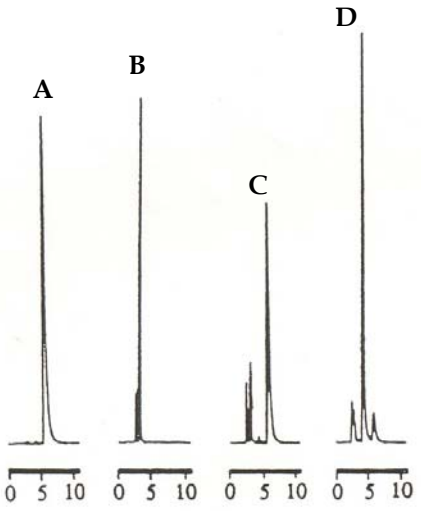

Fig. 1: Chromatograms of Taxol 1.2 mg/mL in 0.9% sodium chloride injection: (A) immediately after preparation, (B) after treatment with 1 N sodium hydroxide 5 hours at 60°C, (C) after treatment with 1 N hydrochloric acid for 5 hours at 60°C, and (D) after treatment with 3% hydrogen peroxide for 12 hours at room temperature. All degradation products of Taxol and various drugs did not interfere with the intact drug in the assay.

Analysis of data

The initial concentration was defined as 100% and subsequent sample concentrations were expressed as percentage of initial concentration. Stability was defined as greater than 90% remaining of the post-admixture drug concentration.

RESULTS AND DISCUSSION

Throughout the study, more than 90% of the initial concentrations of Taxol with either ondansetron, ranitidine, vancomycin or cephalosporins remained in the solutions (Tables 1 to 4). Specifically, Taxol 0.3 mg/mL in 5% dextrose injection maintained a mean relative concentration of at least 94.1% (Table 1) with ondansetron 0.1 mg/mL. Taxol 1.2 mg/mL in 5% dextrose injection maintained a mean relative concentration of at least 95.9% (Table 2) with cefotaxime sodium 20 mg/mL.

Taxol 0.3 mg/mL in 0.9% sodium chloride injection maintained a mean relative concentration of at least 94.4% (Table 3) with cephradine 20 mg/mL. Taxol 1.2 mg/mL in 0.9% sodium chloride injection maintained a mean relative concentration of at least 94.6% (Table 4) with cephradine 20 mg/mL. No precipitates, color changes, or haziness was seen. The changes in pH were minor (Table 5).

Table 1: Stability of Taxol 0.3 mg/mL with ondansetron, ranitidine, vancomycin and cephalosporins in 5% dextrose injection during simulated Y-site administration

Taxol 0.3 mg/mL with drugs	Initial concentration (mg/mL)[a,b]	% of Initial concentration remaining[b]			
		1 h	2 h	4 h	12 h
ondansetron 0.03 mg/mL	0.148±0.012	100.2±1.2	99.9±2.1	98.5±1.6	96.8±1.5
ondansetron 0.1 mg/mL	0.144±0.021	100.8±1.7	99.1±0.6	100.1±1.7	94.1±1.8
ondansetron 0.3 mg/mL	0.146±0.019	10.1.4±1.9	97.9±2.9	96.8±1.8	98.2±0.8
ranitidine 0.5 mg/mL	0.141±0.013	99.2±1.7	96.4±1.7	96.5±1.1	95.9±1.6
ranitidine 2 mg/mL	0.150±0.021	98.3±1.1	97.1±2.1	96.7±1.5	97.1±1.1
vancomycin 1 mg/mL	0.144±0.003	99.3±1.7	100.1±2.8	99.6±1.9	97.4±2.5
vancomycin 5 mg/mL	0.162±0.004	99.6±1.8	99.7±0.9	98.9±0.7	96.2±2.4
vancomycin 10 mg/mL	0.152±0.002	99.7±0.9	99.5±1.2	99.3±0.9	95.3±2.7
ceftezole sodium 20 mg/mL	0.146±0.005	99.6±1.7	98.6±1.9	96.6±2.2	95.2±1.5
cephradine 20 mg/mL	0.151±0.010	98.6±2.2	98.8±2.2	97.4±2.7	96.7±1.2
cefamandole sodium 20 mg/mL	0.155±0.006	98.2±1.6	97.5±1.7	98.0±1.9	97.4±0.9
cefmetazole sodium 20 mg/mL	0.149±0.003	102.3±1.9	99.7±1.9	96.4±1.3	95.2±1.9
cefoperazone sodium 20 mg/mL	0.145±0.008	97.8±3.4	98.7±3.4	96.6±1.1	97.7±2.4
cefotaxime sodium 20 mg/mL	0.145±0.008	97.8±3.4	98.7±3.4	96.6±1.1	97.7±2.4
cefepime hydrochloride 20 mg/mL	0.145±0.007	99.7±1.7	97.2±2.0	95.5±2.1	95.7±1.7

[a]After 1 : 1 dilution with two drugs. [b]Mean ± S.D., n = 3

Table 2: Stability of Taxol 1.2 mg/mL with ondansetron, ranitidine, vancomycin and cephalosporins in 5% dextrose injection during simulated Y-site administration

Taxol 1.2 mg/mL with drugs	Initial concentration (mg/mL) [a,b]	% of Initial concentration remaining[b]			
		1 h	2 h	4 h	12 h
ondansetron 0.03 mg/mL	0.589±0.065	99.1±2.1	98.5±2.6	98.1±1.8	98.5±1.6
ondansetron 0.1 mg/mL	0.577±0.069	98.4±0.9	99.1±1.5	98.2±2.1	96.4±1.8
ondansetron 0.3 mg/mL	0.614±0.075	101.2±1.8	98.0±0.9	99.1±1.9	97.4±2.6
ranitidine 0.5 mg/mL	0.534±0.056	98.6±0.8	97.1±1.2	97.2±1.1	95.4±1.6
ranitidine 2 mg/mL	0.574±0.045	98.2±1.2	96.7±0.8	98.1±1.2	96.7±2.0
vancomycin 1 mg/mL	0.654±0.026	100.3±1.8	101.6±1.4	99.5±1.4	96.9±2.0
vancomycin 5 mg/mL	0.655±0.014	99.4±1.8	99.6±1.2	97.8±1.7	97.2±2.0
vancomycin 10 mg/mL	0.646±0.020	99.4±0.8	99.6±0.9	99.7±1.8	98.7±1.8
ceftezole sodium 20 mg/mL	0.588±0.019	97.6±1.1	98.0±1.8	97.5±2.4	96.7±0.8
cephradine 20 mg/mL	0.592±0.025	98.2±1.9	99.2±2.9	98.2±2.9	97.5±2.0
cefamandole sodium 20 mg/mL	0.579±0.027	99.7±2.2	98.2±3.8	95.7±1.9	95.7±2.4
cefmetazole sodium 20 mg/mL	0.621±0.032	102.4±3.0	98.6±2.0	98.7±3.7	97.8±1.9
cefoperazone sodium 20 mg/mL	0.611±0.011	108.1±2.8	99.9±2.7	98.7±2.6	97.8±1.7
cefotaxime sodium 20 mg/mL	0.578±0.030	98.7±2.4	97.6±1.3	97.2±2.8	95.9±1.1
cefepime hydrochloride 20 mg/mL	0.627±0.021	99.1±1.8	98.7±2.7	99.0±1.7	96.5±2.5

[a]After 1 : 1 dilution with two drugs. [b]Mean ± S.D., n = 3

Table 3: Stability of Taxol 0.3 mg/mL with ondansetron, ranitidine, vancomycin and cephalosporins in 0.9% sodium chloride injection during simulated Y-site administration

Taxol 0.3 mg/mL with drugs	Initial concentration (mg/mL) [a,b]	% of Initial concentration remaining[b]			
		1 h	2 h	4 h	12 h
ondansetron 0.03 mg/mL	0.145±0.021	99.2±2.0	98.2±1.7	97.5±3.1	97.1±1.8
ondansetron 0.1 mg/mL	0.162±0.032	101.7±2.9	98.9±2.9	98.8±1.8	97.1±2.4
ondansetron 0.3 mg/mL	0.141±0.028	98.9±1.4	97.1±1.2	97.6±118	97.0±1.5
ranitidine 0.5 mg/mL	0.143±0.014	98.2±1.9	96.1±1.2	95.5±2.1	96.0±1.3
ranitidine 2 mg/mL	0.155±0.031	99.3±2.1	96.2±2.0	96.8±1.4	96.3±1.4
vancomycin 1 mg/mL	0.146±0.005	98.5±1.8	99.8±2.1	97.9±2.1	96.6±2.9
vancomycin 5 mg/mL	0.164±0.004	98.5±1.1	98.4±1.2	97.5±0.9	97.6±2.4
vancomycin 10 mg/mL	0.159±0.003	99.6±1.5	101.6±1.8	98.2±1.0	97.2±1.1
ceftezole sodium 20 mg/mL	0.141±0.008	99.5±2.3	98.6±1.7	96.6±2.7	95.7±2.7
cephradine 20 mg/mL	0.148±0.005	102.5±1.4	97.9±3.0	96.7±4.1	94.4±2.4
cefamandole sodium 20 mg/mL	0.152±0.006	98.6±1.7	101.0±1.8	96.7±1.2	96.4±2.6
cefmetazole sodium 20 mg/mL	0.159±0.012	99.2±1.0	97.8±2.0	96.7±0.9	94.9±1.9
cefoperazone sodium 20 mg/mL	0.155±0.006	100.9±2.9	98.7±1.7	98.7±1.3	97.7±2.2
cefotaxime sodium 20 mg/mL	0.146±0.005	97.9±2.7	99.5±2.1	96.7±1.5	96.4±1.4
cefepime hydrochloride 20 mg/mL	0.156±0.003	98.1±1.3	99.7±2.4	97.7±2.9	95.5±3.0

[a]After 1 : 1 dilution with two drugs. [b]Mean ± S.D., n = 3

Table 4: Stability of Taxol 1.2 mg/mL with ondansetron, ranitidine, vancomycin and cephalosporins in 0.9% sodium chloride injection during simulated Y-site administration

Taxol 1.2 mg/mL with drugs	Initial concentration (mg/mL) [a,b]	% of Initial concentration remainning[b]			
		1 h	2 h	4 h	12 h
ondansetron 0.03 mg/mL	0.597±0.050	98.9±2.2	96.1±1.9	97.9±2.9	95.6±3.4
ondansetron 0.1 mg/mL	0.623±0.081	97.6±1.3	98.4±2.5	96.7±2.9	96.2±1.4
ondansetron 0.3 mg/mL	0.578±0.088	99.9±2.4	98.8±2.1	98.8±1.1	96.6±3.3
ranitidine 0.5 mg/mL	0.652±0.018	97.9±2.0	96.1±1.4	96.9±1.2	95.7±1.5
ranitidine 2 mg/mL	0.653±0.034	98.1±1,8	97.2±1.5	96.6±0.9	98.1±1.8
vancomycin 1 mg/mL	0.658±0.014	101.2±1.7	98.5±2.9	98.4±2.1	95.5±1.2
vancomycin 5 mg/mL	0.651±0.010	97.6±1.8	98.3±1.7	96.2±1.8	96.3±2.8
vancomycin 10 mg/mL	0.644±0.017	100.5±1.2	99.5±1.0	97.8±1.1	97.4±2.1
ceftezole sodium 20 mg/mL	0.604±0.015	99.6±1.1	96.7±2.7	98.8±1.9	97.8±2.5
cephradine 20 mg/mL	0.624±0.025	98.1±2.7	98.9±2.2	95.6±1.8	94.6±1.1
cefamandole sodium 20 mg/mL	0.599±0.037	99.6±1.7	100.2±2.7	96.3±1.5	98.6±0.9
cefmetazole sodium 20 mg/mL	0.608±0.022	104.8±1.8	99.7±2.1	98.5±1.9	97.8±1.8
cefoperazone sodium 20 mg/mL	0.624±0.019	100.0±0.8	99.3±2.7	97.5±2.0	95.0±2.2
cefotaxime sodium 20 mg/mL	0.568±0.016	97.5±2.3	98.5±1.7	96.7±1.7	96.7±3.0
cefepime hydrochloride 20 mg/mL	0.588±0.023	99.8±2.3	98.7±3.8	97.8±2.7	96.5±1.5

[a]After 1 : 1 dilution with two drugs. [b]Mean ± S.D., n = 3

Table 5: pH of 5% dextrose injection and 0.9% sodium chloride injection containing both of Taxol 1.2 mg/mL and ondansetron, ranitidine, vancomycin or cephalosporins

Taxol 1.2 mg/mL with drugs	pH in 5% dextrose injection [a]			pH in 0.9% sodium chloride injection [a]		
	Initial	4 h	12 h	Initial	4 h	12 h
ondansetron 0.03 mg/mL	6.89±0.11	6.77±0.09	6.28±0.05	6.45±0.02	6.59±0.05	6.67±0.03
ondansetron 0.1 mg/mL	6.67±0.04	6.54±0.04	6.59±0.10	6.76±0.03	6.64±0.11	6.49±0.05
ondansetron 0.3 mg/mL	6.34±0.04	6.24±0.07	6.28±0.04	6.49±0.18	6.57±0.08	6.33±0.03
ranitidine 0.5 mg/mL	6.25±0.18	6.05±0.08	6.02±0.07	6.49±0.07	6.68±0.07	6.69±0.04
ranitidine 2 mg/mL	6.75±0.08	6.74±0.09	6.69±0.11	6.77±0.04	6.69±0.10	6.51±0.02
vancomycin 1 mg/mL	6.34±0.18	6.24±0.08	6.28±0.04	6.49±0.18	6.57±0.08	6.33±0.13
vancomycin 5 mg/mL	6.89±0.11	6.77±0.18	6.28±0.15	6.45±0.12	6.59±0.15	6.67±0.13
vancomycin 10 mg/mL	6.23±0.10	6.21±0.11	6.30±0.09	6.54±0.08	6.48±0.19	6.37±0.14
ceftezole sodium 20 mg/mL	6.32±0.10	6.21±0.11	6.30±0.09	6.14±0.08	6.12±0.18	6.09±0.09
cephradine 20 mg/mL	6.68±0.08	6.54±0.09	6.59±0.11	6.32±0.19	6.22±0.16	6.18±0.05
cefamandole sodium 20 mg/mL	6.51±0.09	6.64±0.11	6.49±0.05	6.19±0.15	6.29±0.11	6.03±0.14
cefmetazole sodium 20 mg/mL	6.62±0.11	6.77±0.18	6.28±0.15	6.07±0.11	6.08±0.09	6.18±0.16
cefoperazone sodium 20 mg/mL	6.59±0.08	6.48±0.19	6.37±0.14	6.18±0.09	6.11±0.13	6.27±0.10
cefotaxime sodium 20 mg/mL	6.17±0.18	6.27±0.20	6.14±0.08	6.28±0.04	6.05±0.19	6.09±0.11
cefepime hydrochloride 20 mg/mL	6.46±0.12	6.49±0.15	6.57±0.13	6.24±0.18	6.29±0.12	6.27±0.09

[a]Mean ± S.D., n = 3

In this study, it is important to avoid common flaws in stability and compatibility studies of inject able drugs (Connors *et al.* 1986; Trissel 1986). Firstly, the drugs and other materials used in the testing should be completely described including sources and quantities or concentrations. Similar products from different suppliers may have different formulations that can affect results. Varying the concentrations may also alter results. All conditions of each test should be included and thoroughly described. Some variables that are not frequently mentioned include the actual temperature, presence or absence of light and container materials. In addition, the analytical methods used should be described in detail and basic items such as pH, color and clarity determined should be described. The materials, test conditions and methods should be described sufficiently well to permit replication of the study.

Secondly, use a stability-indicating assay. The most common flaw is the failure to use an analytical method that has been demonstrated to be stability-indicating (Trissel and Flora 1988). It is incumbent on researchers to demonstrate that the methods they are using will detect and separate the intact drug in the presence of its decomposition products and other drugs and components. Thirdly, perform an analytical determination at the outset. A time-zero determination of drug concentration is essential. Without such a determination of initial concentration, there is no

definitely known starting point. Fourthly, use replicate assays at adequate and appropriate intervals. Multiple assays of test solutions should be performed initially and at all test intervals. Performing several determinations on replicate test solutions at each interval will help to increase confidence in the accuracy of the results obtained by minimizing the effects of assay variability and human error.

As a general rule, duplicate assay of three replicate test solutions are considered a minimum. If these problems are avoided at the outset in the design of the study and through project completion and writing of the paper, much wasted effort will be eliminated and higher quality papers on drug stability and compatibility will result.

CONCLUSION

Taxol 0.3 mg/mL and 1.2 mg/mL in 5% dextrose injection maintained a mean relative concentration of at least 94.1% with various drugs. Taxol 0.3 mg/mL and 1.2 mg/mL in 0.9% sodium chloride injection maintained a mean relative concentration of at least 94.4% with various drugs. Taxol in concentrations of 0.3 and 1.2 mg/mL was stable when mixed with either ondansetron (0.03, 0.1 or 0.3 mg/mL, as the hydrochloride salt), ranitidine (0.5 or 2.0 mg/mL, as the hydrochloride salt), vancomycin (1, 5 or 10 mg/mL, as the hydrochloride salt) or cephalosporins 20 mg/mL in 5% dextrose injection and 0.9% sodium chloride injection during simulated Y-site administration and stored in glass containers for 12 hours. No precipitates, color changes, or haziness was seen. The changes in pH were minor.

REFERENCES

ALLEN, L. V. & STILES, M. L. (1981) Compatibility of various admixtures with secondary additives at Y injection sites of intravenous administration sets, Part 2, *American Journal of Hospital Pharmacy*, 38: 380–381.

ALLEN, L. V., LEVINSON, R. S. & PHISUTSINTHOP, D. (1977) Compatibility of various admixtures with secondary additives at Y injection sites of intravenous administration sets, *American Journal of Hospital Pharmacy,* 34: 939–943.

BOYLE, D. A. & GOLDSPIEL, B. R. (1998) A review of taxol administration, stability, and compatibility issues, *Clinical Journal of Oncology Nursing*, 2: 141–145.

BURM, J. P., CHOI, J. S. & GILL, M. A. (1994) Stability of Taxol and fluconazole during simulated Y-site administration, *American Journal of Hospital Pharmacy,* 51: 2704–2706.

CONNORS, K. A., AMIDON, G. L. & STELLA, V. J. (1986) *Chemical Stability of Pharmaceuticals: A Handbook for Pharmacists*, 2nd Ed., pp. 34–38 (New York: John Wiley).

DONEHOWER, R. C., ROWINSKY, E. K. & GROCHOW, L. B. (1987) Phase I trial of paclitaxel in patients with advanced cancer, *Cancer Treatment Reports,* 71: 1171–1177.

GUNDLACH, C. A., FAULKNER, T. P. & SOUNEY, P. F. (1991) Drug usage patterns in the ICU: Profile of a major metropolitan hospital and comparison with other ICUs, *Hospital Formulary,* 1: 132–136.

ROWINSKY, E. K., CAZENZVE, L. A. & DONEHOWER, R. C. (1990) Paclitaxel: A novel investigational antineoplastic agent, *Journal of the National Cancer Institute,* 82: 1247–1253.

SAUTOU-MIRANDA, V., BRIGAS, F., VANHEERSWYNGHELS, S. & CHOPINEAU, J. (1999) Compatibility of paclitaxel in 5% glucose solution with ECOFLAC low-density polyethylene containers-stability under different storage conditions, *International Journal of Pharmaceutics*, 1: 77–82.

TRISSEL, L. A. (1986) *Handbook on Injectable Drugs*, 4th Ed., pp. 129–132 (Bethesda: American Society of Hospital Pharmacists).

TRISSEL, L. A. & FLORA, K. P. (1988) Stability studies: Five years later, *American Journal of Hospital Pharmacy*, 45: 1569–1571.

TRISSEL, L. A. & BREADY, B. B. (1992) Turbidimetric assessment of the compatibility of the paclitaxel with selected other drugs during simulated Y-site injection, *American Journal of Hospital Pharmacy,* 49: 1716–1719.

TRISSEL, L. A. & MARTINEZ, J. F. (1993) Turbidimetric assessment of the compatibility of paclitaxel with 42 other drugs during simulated Y-site injection, *American Journal of Hospital Pharmacy,* 50: 300–304.

TRISSEL, L. A., XU, Q. A. & GILBERT, D. L. (1998) Compatibility and stability of paclitaxel combined with doxorubicin hydrochloride in infusion solutions, *Annals of Pharmacotherapy*, 32: 1013–1016.

VENKATARAMANAN, R., BURKART, G. J. & PTACHCINSKI, R. J. (1981) Leaching of diethylhexylphthalate from polyvinyl chloride bags into intravenous cyclosporine solutions, *American Journal of Hospital Pharmacy,* 43: 2800–2802.

WALL, M. E. & WANI, M. C. (1977) Antineoplastic agents from plants, *Annual Review of Pharmacology,* 17: 117–132.

WAUGH, W. N., TRISSEL, L. A. & STELLA, V. J. (1991) Stability, compatibility and plasticizer extraction of paclitaxel (NSC-125973) injection diluted in infusion solutions and stored in various containers, *American Journal of Hospital Pharmacy,* 48: 1520–1524.

ZHANG, Y., XU, Q. A., TRISSEL, L. A., GILBERT, D. L. & MARTINEZ, J. F. (1997) Compatibility and stability of paclitaxel combined with cisplatin and with carboplatin in infusion solutions, *Annals of Pharmacotherapy*, 31: 1465–1470.