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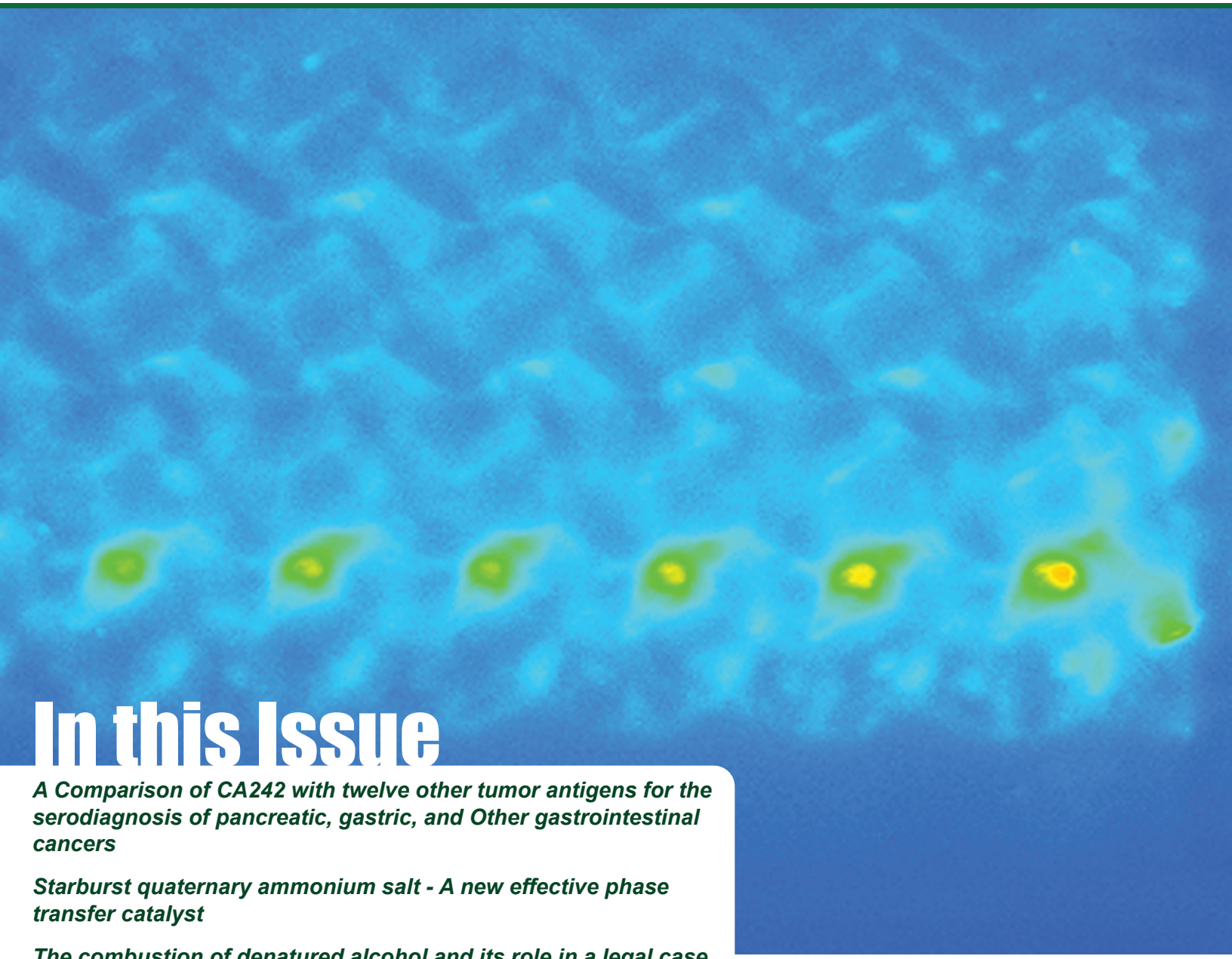

In this Issue

Note: Lab-on-a-Chip; Microfluidics.
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The Chemist

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The Chemist (Established in 1923)

Editorial

Chemistry on the March

David Devraj Kumar
Florida Atlantic University

Earlier this year in my editorial I expressed optimism about the future of chemistry and I continue to stand on it. The advancements in chemical sciences and the applications of chemistry in other areas of science and technology are mind-boggling. Chemistry helps molecular biologists solve complex problems, leads to better understanding of biological systems, and enables environmental scientists to understand and to suggest solutions to environmental issues.

Margot Hall and co-authors report a very important study comparing cancer antigens in diagnosing pancreatic, gastric and other gastrointestinal cancers. According to their findings CA 195 seems to be the best with CA 19-9, CA 50, and CA 242 for the detection of pancreatic cancer, and with CA 242 and CA 50 for the detection of gastric cancer. I hope their findings will lead to the development of procedures for the early detection of these cancers so that proper treatments can be implemented.

Divia N and co-authors report the synthesis 3,5-Bis((2-methyl-naphthalene-1-yl)-phenyl-amino-phenyl)-butyl-(2-methoxy-naphthalene-1-yl)-phenylammoniumbromide (BPBPB) and its application as an efficient catalyst for certain organic reactions. David Manuta discusses a complicated legal case involving the combustion of denatured alcohol exposing the chemistry of certain colognes.

John Hill and co-author explore ways to implement the "Chemistry for All" vision initiated by the International Union of Pure and Applied Chemistry in order to overcome `chemophobia' by empowering the general public to understand the role of chemistry in the complex world in which they live. On the other hand, chemistry in the wrong hands for wrong motives is counterproductive.

James Smith argues in his eye-opening article that in the field of environmental forensics the peer-review process is being taken advantage of to establish expertise in litigations involving environmental issues. However, who is going to play gatekeeper to stop misuse of the peer review process in an age where poorly managed open-access journals run by for-profit industries with unknown whereabouts is a very important question.

Sue Rao makes an attempt to raise public awareness and understanding of the science of e-cigarettes. Kim Cavendish and Madelyn Reus briefly outline chemistry activities at the Museum of Discovery and Science in Fort Lauderdale. Fatimah Unnisa and Margot Hall offer thoughtful reviews of the instructors DVD of *Lehninger Principles of Biochemistry* (6^{th} edition) and the book *Goldfrank's Toxicology Emergencies* (9^{th} edition).

It is impossible to edit and re-launch this important scholarly journal without the support of Dean Valerie Bristor at Florida Atlantic University providing a home base. Also, I would like to acknowledge the voluntary efforts of reviewers from the journal's Editorial Review Board and of invited guest reviewer Dr. Penelope Fritzer at Florida Atlantic University. All these reviewers graciously provided timely and thoughtful reviews of manuscripts, thus enhancing the quality of this issue of *The Chemist*.

Thank you.

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A Comparison of CA242 with Twelve Other Tumor Antigens for the Serodiagnosis of Pancreatic, Gastric, and Other Gastrointestinal Cancers

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Abstract: The objective of this study was the comparison of CA 242 with twelve other cancer antigens for its usefulness in the diagnosis of pancreatic, gastric, and other gastrointestinal cancers. Sera from 554 patients (16 pancreatic cancer, 12 gastric cancer, 116 other gastrointestinal cancer, 215 other cancer, and 195 non-cancer) seen in a local hospital were assayed for carcinoembryonic antigen (CEA), CA 19-9, CA 195, CA 50, CA 242, CA 72-4, ferritin, CA 125, CA 15-3, CA 27.29, alpha fetoprotein (AFP), Cyfra 21-1, and neuron specific enolase (NSE). Diagnostic sensitivities for pancreatic and gastric cancers respectively were: CEA (37.5%, 50.0%), CA 19-9 (66.7%, 63.6%) , CA 195 (100%, 58.3%), CA 50 (66.7%, 70.0%), CA 242 (66.7%, 70.0%), CA 72-4 (31.3%, 27.3%), ferritin (50.0%, 11.1%), CA 125 (40.0%, 40.0%), CA 15-3 (26.7%, 45.5%), CA 27.29 (40.0%, 30.0%), AFP (18.2%, 22.2%), Cyfra 21-1 (26.7%, 9.1%), and NSE (0.0%, 0.0)%). Diagnostic specificities and efficiencies were above 74% for all antigens and both cancers. Especially noteworthy was the fact that 9/16 pancreatic cancer and 6/12 gastric cancer patients had a CA 195 concentration which was greater than 20x the upper limit of normal (ULN). Two of the pancreatic cancer patients had CA 195 concentrations above 1000x ULN prior to their diagnosis by conventional methods (imaging and biopsy). CA 242 and CA 50 were superior to the other markers for the detection of gastric cancer. CA 195 proved the best with CA 19-9, CA 50, and CA 242 also proving excellent for the detection of pancreatic cancer.

[4] **Nonstandard Abbreviations:** CEA, carcinoembryonic antigen; AFP, alpha fetoprotein; CA 195, cancer antigen 195; CA 19-9, cancer antigen 19-9; CA 50, cancer antigen 50; CA242, cancer antigen 242; CA72-4, cancer antigen 72-4; CA 125, cancer antigen 125; CA 15-3, cancer antigen 15-3; CA 27.29, cancer antigen 27.29; Cyfra 21-1, cytokeratin fragment 19; NSE, neuron specific enolase; ferritin.

Key Words: Tumor Antogens, Serodiagnosis, Pancreatic Cancer, Gastric Cancer, Gatrointestinal Cancer.

INTRODUCTION

Gastrointestinal (GI) cancer is an important medical problem. The American Cancer Society estimates that during 2006 there were 263,060 new cases and 136,180 deaths due to all GI cancers in the USA. These figures include new cases (22,280; 33,730) and deaths (11,430; 32,300) due to gastric and pancreatic cancer respectively (1). Similarly, the World Health Organization (2) indicates that gastric cancer is the fourth most prevalent cancer globally and the most prevalent cancer in less developed nations while pancreatic cancer ranks only ninth (2) globally; it has a five year survival rate of less than 10% (3), making it a deadly disease. The late diagnosis of pancreatic cancer contributes substantially to its poor prognosis and low survival rate. Hence there is a real need for a minimally invasive early diagnostic method (3).

Traditional methods of gastrointestinal cancer diagnosis have included guaiac tests for occult blood, biopsy, exfoliative cytology, endoscopy, barium X-rays, ultrasonography, computer tomography (CAT scans), and magnetic resonance imaging (MRI). Ultrasonography, CAT scans and MRIs, taken in combination with the clinical presentation, have proven the most valuable for the diagnosis of pancreatic cancer (3-4). Additionally, serum tumor antigens have been used as a diagnostic aid to measure tumor burden, and to detect recurrent disease and monitor therapy for pancreatic and other gastrointestinal cancers (5-6). Tumor antigens that have proven useful for the detection of a variety of gastrointestinal cancers include among others: CEA, CA 19-9, CA 72-4, CA 50, CA 195, and CA242. The principal tumor marker in current use for the diagnosis and monitoring of pancreatic cancer is CA 19-9. Likewise, CA 72-4 and CEA are the major tumor antigens associated with gastric cancer and colorectal cancer, respectively (5). Elevated alpha-fetoprotein (AFP) has been extensively used as a marker for hepatic disease, including hepatoma, and for yolk sac-derived germ cell tumors. It has also been reported in a few cases of other gastrointestinal cancers (5-7). CA125 is a marker of ovarian cancer, but has been reported to have some sensitivity for gastrointestinal cancer (5, 8). Elevated CA 15-3 has been reported in a variety of adenocarcinomas, including breast, lung, ovary, colon, and pancreas. It is principally used in the assessment of breast cancer patients (9). CA27.29 is used as a marker for therapeutic monitoring in breast cancer patients (10-11). It has also been reported in some cases of ovarian, uterine, lung, prostate, colorectal, and pancreatic cancer (12). Cyfra 21-1 is used as a marker of lung cancer and has not been reported to be useful in diagnosis and monitoring of gastrointestinal cancer (5, 13). There are reports of elevated serum ferritin levels in patients with hematological cancers, hepatocellular carcinoma, and cancer of the esophagus, pancreas, colon, breast, lungs, and ovaries. (5, 14). Neuron specific enolase (NSE) is used as a marker for small cell lung carcinoma, neuroblastoma and some renal tumors. It has also been reported to be elevated in colorectal and gastric cancers as well as endocrine pancreatic tumors, oatcell cancer, seminoma, melanoma, and medullary thyroid cancer (5) and pheochromocytoma and carcinoid tumors (14).

CEA is a 150-300 kDa cell surface heterogeneous glycoprotein which is structurally similar to IgG. Abnormally elevated serum levels have been reported in patients with colorectal cancer, breast cancer, and a variety of other carcinomas (15-16). Additionally, CEA levels can be elevated in heavy smokers and patients with nonmalignant pathologies (17). Consequently, CEA is currently used in therapeutic monitoring and as a diagnostic aid, but is not useful in screening for cancer. It has long been considered to be the "gold standard" for the detection of gastrointestinal diseases.

CA 19-9 is a high molecular weight (200-1000 kDa) mucin like glycoprotein which exists as a ganglioside on tumor cells. The expression of this sialylated Le^a blood group antigen (sialylated lacto-N-fucopentoeose II ganglioside) is required for the expression of CA 19-9 and hence, Le^{a-b-} patients do not express the antigen and can present as false negatives (18). A monoclonal antibody was developed against CA 19-9 derived from the SW-1116 human colon carcinoma cell line (19). CA 19-9 is clinically useful in the detection of pancreatic, colorectal, hepatic, and other gastrointestinal cancers. It has also been described in breast and lung cancer (5). CA 50 is related to CA 19-9, but lacks a fucose residue. Its epitope is the same as that found in Le^{a-b-} (Lewis negative) patients. It has been reported in patients with gastric, colon, and hepatic cancer (20). CA 195 is also related to CA 19-9. It is defined by the mouse monoclonal antibody CC3C-195 and it recognizes both Le^a and sialyl-Le^a epitopes. Binding with higher affinity to the sialylated Le^a blood group antigen, the antibody can bind to both the sialylated and unsialylated Le^a blood group. CA 195 has been reported in pancreatic, colon, and gastric cancers (5).

CA 242 is also related to CA 19-9 and CA 50 (21). A mouse monoclonal antibody (CA242) directed at COLO 205 (a human colorectal cancer cell line) and a second antibody directed against sialylated Lewis A detect this antigen (14). CA 242 has been reported in pancreatic, (22), colorectal (23), gastric and liver cancers (21).

CA 72-4 is a 1 million kDa mucin-like glycoprotein complex (TAG 72), which is predominantly associated with human adenocarcinoma of the gastrointestinal tract (24-25). Two monoclonal antibodies (cc49 and B72.3) have been developed against it which detect distinct antigenic determinants expressed on the circulating antigen found in a variety of gastrointestinal cancers and lung cancer (26-27). Its use is recommended in cases of gastric cancer and it has been used in tumor panels (ratio of CA 19-9 to CA 72.4) to exclude pancreatic disease (5).

CA 125 is a 200 kDa glycoprotein expressed by tissue of mullerian duct origin as well as by ovarian tumors. It is defined by the mouse monoclonal antibody OC 125 derived from an ovarian cancer cell line (OVCA 433). It is

currently used for detecting epithelial tumors of the ovary. However, it has also been reported in breast, lung, endometrial, and gastrointestinal tumors. It can be elevated with pregnancy and with pelvic inflammatory disease (28).

CA 15-3 is a 300-450 kDa glycoprotein defined by two monoclonal antibodies. The 115D8 antibody recognizes human milk fat globule membranes and the DF3 antibody reacts with a breast cancer antigen extract (29-30). It is principally used to monitor breast cancer patients, but has been reported in cases of ovarian, pancreatic, lung, and colorectal cancer (5). CA 27.29 is a mucin antigen defined by the monoclonal antibody B27.29. This antibody recognizes an antigen extracted from ascites fluid derived from patients with breast cancer. CA 27.29 has an epitope that is shared with the DF3 antibody of CA15-3 (31). It is currently being marketed as a specific test for breast cancer, however it has been reported in some cases of ovarian, uterine, lung, prostate, colorectal, and pancreatic cancer (32).

Alpha-fetoprotein (AFP) is a 70,000 kDa glycoprotein which has been isolated from patients with hepatocellular carcinomas and germ cell tumors (33). Maternal serum and amniotic fluid AFP levels are routinely used for the prenatal diagnosis of open neural tube disease and gastroschisis, and together with karyotyping have been used to diagnose cases of Down's Syndrome (34-35). Alpha-fetoprotein has been reported to be useful in screening for hepatocellular carcinoma in high incidence areas such as Asia, and for classifying and staging germ cell tumors (33). AFP has been reported in hepatocellular carcinoma, testicular and ovarian germ cell tumors, as well as pancreatic, colorectal and gastric carcinomas (7).

Ferritin is a 460 kDa intracellular apoprotein that when saturated with iron forms a storage protein of approximately 900 kDa. (36-37). Serum ferritin levels reflect the total iron stores of the patient (37). Increased serum ferritin is also observed in hepatocellular carcinoma (14), acute myelocytic leukemia, Hodgkin's lymphoma, neuroblastoma, teratoblastoma and cancers of the colon, esophagus, breast, lungs, and ovaries (5).

Cyfra 21-1 is a 40 kDa fragment derived from cytokeratin 19. One subgroup of intermediate filament proteins, cytokeratins are found in epithelial cells. The monoclonal antibody recognizes an epitope on the Cyfra 21-1 fragment and is useful in the detection of non-small cell lung cancer, including squamous cell carcinoma of the lung (38). It has also been reported in patients with cervical cancer and other malignancies (39-40).

Neuron specific enolase (NSE) is a 78 kDa glycolytic isoenzyme (14). Elevated serum NSE levels have been observed in cancers of neuroendocrine origin. These include small cell lung cancer (SCLS), neuroblastoma, pheochromocytoma, melanoma, medullary thyroid cancer, intestinal carcinoids, and pancreatic endocrine tumors. (31, 5). It is primarily used in the assessment of SCLC (14).

The purpose of this study was to compare the analytical and clinical performances of thirteen serologic tumor marker tests (CEA, CA 19-9, CA 195, CA 50, CA 242, ferritin, CA 72-4, CA 125, CA15-3, CA 27.29, AFP, Cyfra 21-1, and NSE) for the detection of pancreatic cancer, gastric cancer, and other gastrointestinal cancers.

MATERIALS & METHODS

ASSAYS

All assays were performed according to the directions supplied by the manufacturers. The Tandem®-E CEA assay (Hybritech, Inc) is a solid phase two-site immunoenzymometric assay utilizing two monoclonal IgG antibodies directed against unique sites on the CEA antigen. This assay was quantitated spectrophotometrically using the Photon Immunoassay Analyzer™ from Hybritech, Inc. The Centocor® CA 19-9™ assay (Fujirebio Diagnostics, Inc./Centocor, Inc.) is a solid phase radioimmunoassay (CA 19-9) using the 1116-NS-19-9 antibody for both the capture and tracer antibodies. This antibody is directed against an epitope, which is biochemically related to the Lewis A determinant; the assay was quantitated using a Genesys™ 5000 gamma counter (Laboratory Technologies, Inc.). The Tandem®- CA 195/Hybri C Mark™ assay (Hybritch Europe, Inc.) is a solid phase two-site immunoradiometric assay (CA 195) utilizing monoclonal IgM antibodies developed against the Lewis A (blood group determinant) and sialyated Lewis A epitopes on the CA 195 antigen. This assay was measured using a Genesys™ 5000 gamma counter (Laboratory Technologies, Inc.). The RIA-gnost® CA-50 assay (CIS bio international) is a solid phase two-site immunoradiometric assay (CA 50) utilizing monoclonal mouse antibodies directed at two carbohydrate chains (sialylated Lewis A and sialylated lactotetraose) of the adenocarcinoma cell line Colo 205. The assay was measured using a Genesys™ 5000 gamma counter (Laboratory Technologies, Inc.). The Diagnostic

Automation® CA242 assay (Diagnostic Automation, Inc) is a solid phase enzyme linked immunosorbent assay (CA 242) based on an antibody (C242) directed against a colorectal carcinoma cell line (COLO 205) and another antibody directed against sialylated Lewis A. The assay results were quantitated using the Bio-Tek EL 800 microtiter plate reader (Bio-Tek, Inc). The Centocor® CA 72-4™ assay (Fujirebio Diagnostics, Inc./Centocor, Inc.) is a solid phase radioimmunoassay (CA 72-4) based on two monoclonal antibodies, cc49 and B72.3, which react with distinct antigenic determinants on a tumor associated glycoprotein TAG 72. The antigen was quantitated using the Genesys™ 5000 gamma counter (Laboratory Technologies, Inc.). The Centocor® CA 125™ assay (Fujirebio Diagnostics, Inc./Centocor, Inc.) is a solid phase two-site immunoradiometric assay (CA 125) using two mouse monoclonal antibodies, OC125 directed against the OVCA 433 ovarian cancer cell line and a second antibody directed against another CA 125 epitope. The assay was measured using a Genesys™ 5000 gamma counter (Laboratory Technologies, Inc.). The Centocor® CA 15-3® assay (Fujirebio Diagnostics, Inc./Centocor, Inc.) is a solid phase radioimmunoassay using the 115D8 murine monoclonal antibody as the capture antibody and the I^{125} labeled DF3 murine monoclonal antibody as the tracer. This assay was quantitated using an Iso Data® gamma counter. The Truquant® BR™ assay (Fujirebio Diagnostics, Inc./Centocor, Inc) is a solid phase competitive inhibition radioimmunoassay using polystyrene tubes coated with CA 27.29 antigen and I^{125} labeled murine monoclonal B27.29 antibody. This assay was quantitated using an Iso Data® gamma counter. The IMx® AFP assay (Abbott Laboratories, Inc.) is a microparticle enzyme immunoassay (MEIA) utilizing two monoclonal antibodies directed against unique sites on the AFP antigen. This assay was quantitated using the IMx® Automated Analyzer from Abbott Laboratories, Inc. The Diagnostic Automation® Ferritin assay (Diagnostic Automation, Inc) is a solid phase enzyme linked immunosorbent (ferritin) assay using two mouse monoclonal antibodies directed at different sites on the protein. This assay was quantitated using the Beckman Coulter™ AD340 microtiter plate reader (Beckman Coulter, Inc.). The Diagnostic Automation® Neuron Specific Enolase (NSE) assay (Diagnostic Automation, Inc) is a solid phase enzyme linked immunosorbent assay which uses two mouse monoclonal antibodies directed at different epitopes of the gamma (γ) subunit of the NSE isoenzyme. This assay was quantitated using the Beckman Coulter™ AD340 microtiter plate reader (Beckman Coulter, Inc). The Centocor® Cyfra™ 21-1 assay (Fujirebio Diagnostics, Inc./Centocor, Inc.) is a solid phase immunoradiometric assay utilizing two mouse monoclonal antibodies, KS19.1 and BM19.21, to detect cytokeratin 19 fragments in serum. The assay was quantitated using a Genesys™ 5000 gamma counter (Laboratory Technologies, Inc.). Statistical analysis was performed using SPSS software.

PATIENTS AND CONTROLS

Procedures used in this study were in accord with ethical standards established by the University of Southern Mississippi (USM). Permission for the study was granted by the USM Human Subjects Protection Review Committee (HSPRC/IRB) and the hospital IRB. All documents relating to the patients, including informed consent, were maintained by the hospital. Patient samples were given a numerical code and patient names were not divulged to the researchers.

All study participants were selected from patients seen in an area hospital. This hospital has a large oncology division. Five hundred and fifty four patients were randomly chosen and the assays were run in a blind fashion. Blood samples were collected using appropriate aseptic technique. Following serum separation aliquots were coded and frozen at -20° C. Subsequently, aliquots were thawed at 37°C and assayed in duplicate (sample permitting) for the tumor antigens. The diagnoses were obtained from the attending physicians and were based on pathological examination. Patient classifications included (a) no known disease, (b) nonmalignant disease, (c) cancer of non-gastrointestinal origin, and (d) specific gastrointestinal cancers. Cancer patients were classified according to the primary site of the tumor, regardless of the presence or absence of metastases.

The normal control subjects were healthy males (~100) and females (~100) ranging from 18-65 years of age. Their blood samples were collected and processed in the same manner as the patient samples.

RESULTS

PRECISION AND LINEARITY

Quality control samples were used to determine intra- and inter-assay precision. The within-run coefficient of variation (%CV) was ` 11% for all but the CA 15-3 (20%) and ferritin (50%) assays which were

higher (Table 1). Similarly the between-run coefficient of variation was equal to or less than 16% for all of the assays except ferritin ((41%)(Table 2). Serial dilutions of abnormal pool samples exhibited good linearity with R^2 values (CEA [0.99], CA 19-9 [0.99], CA 195 [0.99], CA 50 [0.99], CA 242 [0.98], CA 72-4 [0.99], ferritin [0.97], CA 125 [0.99], CA 15-3 [0.99], CA 27.29 [0.99], AFP [0.99], NSE [0.88], Cyfra 21-1 [0.99]) equal to or greater than 0.97 for all the assays except NSE (0.88).

Table 1. Within-run Precision for CEA, CA 19-9, CA 195, CA 50, CA 242, CA 72-4, Ferritin, CA 125, CA 15-3, CA 27.29, AFP, Cyfra 21-1 and NSE

Sample	n	Mean	SD	CV (%)
CEA Low Control	43	4.28 µg/L	0.29	6.78
CEA High Control	40	64.04 µg/L	2.79	4.36
CA 19-9 Low Control	20	39.66 kU/L	2.18	5.51
CA 19-9 High Control	20	76.28 kU/L	4.79	6.28
CA 195 Low Control	30	11.60 kU/L	1.10	9.53
CA 195 Mid Control	30	52.30 kU/L	3.55	6.80
CA 195 High Control	30	79.40 kU/L	7.24	9.13
CA 50 Low Control	20	12.78 kU/L	0.58	4.54
CA 50 High Control	20	100.45 kU/L	4.18	4.16
CA 242 Control	20	72.07 kU/L	7.40	10.27
CA 72-4 Low Control	20	9.24 kU/L	0.74	8.05
CA 72-4 High Control	20	69.66 kU/L	3.57	5.13
Ferritin Control	62	45.74 µg/L	22.80	49.85
CA 125 Low Control	20	55.16 kU/L	3.48	6.31
CA 125 High Control	20	101.39 kU/L	6.38	6.29
CA 15-3 Control	50	46.83 kU/L	9.60	20.50
CA 27.29 Control I	42	75.36 kU/L	6.61	8.77
CA 27.29 Control II	37	106.51 kU/L	9.93	9.32
AFP Low Control	10	20.36 µg/L	2.22	10.90
AFP Medium Control	10	77.87 µg/L	3.16	4.06
AFP High Control	10	171.22 µg/L	4.96	2.90
Cyfra 21-1 Low Control	20	4.41 µg/L	0.28	6.27
Cyfra 21-1 High Control	20	14.17 µg/L	0.77	5.41
NSE Control	10	7.55 µg/L	0.21	2.78

Table 2. Between-run Precision for CEA, CA 19-9, CA 195, CA 50, CA 242, CA 72-4, Ferritin, CA 125, CA 15-3, CA 27.29, AFP, Cyfra 21-1 and NSE

Sample	n	Mean	SD	CV (%)
CEA Low Control	76	4.44 µg/L	0.37	8.33
CEA High Control	72	62.64 µg/L	3.40	5.43
CA 19-9 Low Control	59	44.57 kU/L	4.33	9.72
CA 19-9 High Control	59	84.85 kU/L	8.65	10.19
CA 195 Low Control	62	11.67 kU/L	1.88	16.11
CA 195 Mid Control	58	52.03 kU/L	4.81	9.25
CA 195 High Control	62	80.68 kU/L	10.39	12.88
CA 50 Low Control	57	12.87 kU/L	0.86	6.68
CA 50 High Control	57	105.46 kU/L	7.73	7.33
CA 242 Control	42	67.82 kU/L	10.52	15.51
CA 72-4 Low Control	65	9.57 kU/L	0.71	7.37
CA 72-4 High Control	66	71.17 kU/L	3.57	5.01
Ferritin Control	98	46.55 µg/L	18.94	40.69
CA 125 Low Control	86	54.08 kU/L	5.50	10.17
CA 125 High Control	86	107.11 kU/L	8.14	7.56
CA 15-3 Control	67	45.21 kU/L	6.61	14.62
CA 27.29 Control I	73	74.99 kU/L	6.95	9.27
CA 27.29 Control II	68	117.76 kU/L	16.38	13.91
AFP Low Control	38	19.60 µg/L	1.44	7.35
AFP Medium Control	38	78.15 µg/L	3.88	4.96
AFP High Control	38	167.01 µg/L	6.28	3.76
Cyfra 21-1 Low Control	78	4.45 µg/L	0.50	11.23
Cyfra 21-1 High Control	76	13.97 µg/L	0.86	6.16
NSE Control	43	7.87 µg/L	1.21	15.37

REFERENCE INTERVALS

The minimum detectable concentration of analyte (analytical sensitivity) was determined by analyzing approximately 20 replicates of the zero calibrator/diluent, calculating the mean plus two standard deviations, and establishing this as the cut-off value (Table 3). Values falling below this cutoff were presumed to be analyte free. The cutoff for CA 125 (6.0 kU/L [U/mL]), ferritin (7 µg/L [ng/mL]), NSE (7 µg/L [ng/mL]) and CA242 (17 kU/L [U/mL]) were higher than expected. Values for the other assays were equal to or less than 3.6 kU/L [U/mL] (Table 6). The normal adult reference intervals were established by determining the 95% confidence intervals for healthy control male and female subjects. The intervals (Tables 4, 5) were broader than those reported by the manufacturer for all but the CA 125, CA 72-4, CA 27.29, AFP, and NSE assays, which were somewhat narrower. There was no significant difference between healthy adult males and females for any of the assays except CA 19-9, where the males were significantly ($p<0.05$) higher.

Table 3, 4, and 5. Reference Intervals for CEA, CA 19-9, CA 195, CA 50, CA 242, CA 72-4, Ferritin, CA 125, CA 15-3, CA 27.29, AFP, Cyfra 21-1, and NSE

Table 3

Sample	n	Mean	SD	Range
Zero/Diluent Controls				
CEA	20	0.00 µg/L	0.35	0.00-0.70
CA 19-9	20	0.00 kU/L	0.70	0.00-1.40
CA 195	20	0.00 kU/L	1.50	0.00-3.00
CA 50	20	0.08 kU/L	0.12	0.00-0.32
CA 242	20	9.57 kU/L	3.72	2.13-17.01
CA 72-4	20	2.93 kU/L	0.36	2.21-3.64
Ferritin	10	0.00 µg/L	3.45	0.00-6.90
CA 125	20	3.20 kU/L	1.44	0.40-6.00
CA 15-3	21	0.02 kU/L	0.08	0.00-0.18
CA 27.29	24	0.24 kU/L	1.16	0.00-2.56
AFP	13	0.00 µg/L	0.01	0.00-0.02
Cyfra 21-1	20	0.01 µg/L	0.03	0.00-0.07
NSE	10	6.56 µg/L	0.23	6.10-7.02

Table 4

Sample	n	Mean	SD	Range
Healthy Adults				
CEA	264	2.82 µg/L	2.64	0.00-8.10
CA 19-9	199	16.01 kU/L	15.53	0.00-47.08
CA 195	230	4.96 kU/L	6.58	0.00-18.11
CA 50	200	14.93 kU/L	13.81	0.00-42.55
CA 242	199	30.01 kU/L	19.61	0.00-69.34
CA 72-4	200	1.32 kU/L	1.09	0.00-3.50
Ferritin	156	184.25 µg/L	180.12	0.00-544.49
CA 125	200	10.60 kU/L	8.58	0.00-27.76
CA 15-3	214	24.71 kU/L	14.00	0.00-52.72
CA 27.29	200	17.74 kU/L	7.42	2.90-32.58
AFP	214	3.60 µg/L	1.93	0.00-7.46
Cyfra 21-1	200	1.00 µg/L	1.90	0.00-4.80
NSE	80	7.73 µg/L	2.93	1.87-13.59

Table 5

Sample Healthy Adult Males	n	Mean	SD	Range
CEA	133	3.08 µg/L	2.36	0.00-7.80
CA 19-9	99	18.73 kU/L	18.67	0.00-56.07
CA 195	121	5.07 kU/L	6.50	0.00-18.07
CA 50	100	14.84 kU/L	15.30	0.00-45.44
CA 242	100	29.48 kU/L	22.39	0.00-74.26
CA 72-4	100	1.41 kU/L	0.91	0.00-3.23
Ferritin	80	180.23 µg/L	187.15	0.00-554.53
CA 125	100	10.44 kU/L	8.26	0.00-26.95
CA 15-3	106	25.36 kU/L	13.92	0.00-53.20
CA 27.29	100	18.94 kU/L	8.28	2.38-35.50
AFP	107	3.47 µg/L	1.79	0.00-7.05
Cyfra 21-1	100	1.02 µg/L	2.06	0.00-5.13
NSE	40	7.24 µg/L	2.00	3.24-11.24
Healthy Adult Females				
CEA	131	2.55 µg/L	2.89	0.00-8.33
CA 19-9	100	13.33 kU/L	11.08	0.00-35.49
CA 195	109	4.83 kU/L	6.69	0.00-18.21
CA 50	100	15.02 kU/L	12.22	0.00-39.46
CA 242	99	30.56 kU/L	16.42	0.00-63.41
CA 72-4	100	1.23 kU/L	1.25	0.00-3.72
Ferritin	76	188.48 µg/L	173.54	0.00-535.56
CA 125	100	10.77 kU/L	8.93	0.00-28.62
CA 15-3	108	24.08 kU/L	14.12	0.00-52.32
CA 27.29	100	16.54 kU/L	6.28	3.98-29.10
AFP	107	3.73 µg/L	2.06	0.00-7.85
Cyfra 21-1	100	0.99 µg/L	1.73	0.00-4.45
NSE	40	8.21 µg/L	3.59	1.03-15.39

Table 6. Comparison of Pancreatic Cancer Patient Results

ID#	CEA µg/L	CA 19-9 kU/L	CA 195 kU/L	CA 50 kU/L	CA 242 kU/L	CA 72-4 kU/L	Ferritin µg/L	CA 125 kU/L	CA 15-3 kU/L	CA27.29 kU/L	AFP µg/L	Cyfra 21-1 µg/L	NSE µg/L
33	48.25	596.10	4270.00	321.40	200.00	1.60	465.14	150.00	35.99	65.40	2.98	28.70	7.98
34	0.16	521.40	526.00	234.40	200.00	1.20	-	340.00	24.76	60.40	-	14.40	-
78	1.34	-	16.10	-	-	5.60	-	-	-	-	-	-	-
92	80.76	278.70	516.00	205.90	200.00	19.00	207.80	70.00	38.80	101.59	2.17	2.10	6.93
229	3.08	10.60	42.30	13.70	20.63	0.80	29.38	13.00	16.63	13.84	3.09	0.00	7.79
268	14.20	593.70	843.00	291.50	200.00	6.50	418.24	22.00	7.88	19.67	14.46	0.00	7.37
270	0.85	11.50	11.40	10.30	27.47	1.00	0.00	21.00	15.20	22.79	3.40	0.00	7.91
287	4.08	493.50	551.00	250.40	200.00	1.70	373.32	218.00	31.23	39.52	2.42	11.80	7.73
301	4.97	46.40	20.60	33.40	18.18	0.20	326.31	26.00	14.99	10.63	14.88	2.50	5.69
309	11.32	464.50	296.50	201.60	144.55	0.70	-	24.00	11.92	9.22	-	1.40	-
343	2.65	7.60	22.70	15.90	20.06	0.20	18.16	19.00	22.08	13.06	2.87	0.00	5.71
344	1.14	13.00	29.30	17.20	11.43	0.00	86.13	0.00	33.82	31.29	3.83	0.00	5.92
386	13.11	652.70	12300.00	424.90	200.00	4.00	693.20	0.00	19.18	24.90	-	3.00	7.23
446	34.45	560.80	11660.00	402.50	200.00	9.80	-	386.00	40.79	39.87	-	95.10	-
462	3.34	20.40	13.80	19.60	77.93	1.30	375.67	0.00	25.20	39.40	6.07	0.30	7.06
500	1.76	528.40	462.00	214.90	130.32	15.10		135.00	59.89	21.64	3.54	1.50	7.04
Cutoffs	5.00	37.00	10.50	25.00	69.00	5.60	M/F 250.00/ 120.00	35.00	35.00	37.7	8.9	4.80	15.00

DIAGNOSTIC PARAMETERS

With the exception of CA242 and ferritin, cutoffs between normal and abnormal test results used in this study were those given by the assay manufacturers and are cited in the table legends. The cutoff used for CA242 was that obtained by our normal reference interval and the ferritin cutoffs for males and females were derived from the literature. The patients' diagnoses were made by the attending physicians and were predicated on a variety of pathologic findings, including the histologic analysis of biopsy or surgical tissue. In the study there were 184 patients without disease, 11 patients with non-malignant disease, 16 patients with pancreatic cancer, 12 patients with gastric cancer, 101 patients with colorectal cancer, and 230 patients with other types of cancer. The other types of cancer included: 2 esophageal, 3 small intestinal, 3 gallbladder, 4 hepatic, 3 cecal, 17 lung, 87 breast, 6 ovarian, 2 uterine, 17 prostatic, 20 testicular, 6 renal, 6 head and neck, 13 leukemia, 16 lymphoma, and 25 all other types.

A comparison of assay results for the pancreatic cancer patients is given in Table 6. The most important finding was that 100% of the patients with pancreatic cancer had abnormally elevated serum CA 195. Especially noteworthy was the fact that 9/16 pancreatic cancer patients had a serum CA 195 concentration which was greater than 20x the upper limit of normal (ULN). Seven of these patients had CA 195 concentrations that were greater than 50 x ULN and two patients had values that were greater than 1000 x ULN prior to their diagnosis by conventional methods (imaging and biopsy). Serum concentrations of all the other tumor antigens were less than 20x ULN in the pancreatic cancer patients.

A comparison of assay results for the gastric cancer patients is given in Table 7. Seventy percent of the CA 242 and CA 50 assay results and 63.6% of the CA 19-9 results were elevated in the gastric cancer patients with serum levels reaching 15x ULN for these assays. For CA 195 there were only 7/12 (58.3%) abnormally elevated assay results. However, four of these patients had serum CA 195 concentrations that were greater than 100x ULN.

Predictive values were calculated for pancreatic cancer (Table 8), gastric cancer (Table 9), and combined gastrointestinal cancer (Table 10). Disease prevalence for the patient population was 2.89% for pancreatic cancer, 2.17% for gastric cancer, and 25.99% for combined gastrointestinal cancers. The number of patients tested varied according to the volume of sample available and is given in the tables.

As a consequence of this, there were minor variations in the disease prevalence for the samples on which each analyte was tested (pancreatic cancer 2.63-3.04%, gastric cancer 1.94-2.17%, combined gastrointestinal cancer 25.82-26.94%).

Table 8 shows that the diagnostic sensitivities of CA 195 (100%), CA 19-9 (66.7%), CA 50 (66.7%), and CA 242 (66.7%) were superior to those of the other assays (18.2-50.0%) for pancreatic cancer.

In Table 9, the diagnostic sensitivities of CA 50 (70.0%), CA 242 (70.0%), CA 19-9 (63.6%), and CA 195 (58.3%) were superior to those of the other markers (9.1-50%) for gastric cancer.

Table 10 gives the predictive values for combined gastrointestinal cancers and reflects the predominance of colorectal cancer patients. The diagnostic sensitivity was less than 50% in each of the assays for combined gastrointestinal cancer (Table 10). These values were similar to those calculated for colorectal cancer (data not shown). The diagnostic specificities of the thirteen assays ranged from 72 - 100% with NSE having the highest value for pancreatic, gastric, and combined gastrointestinal cancers (Tables 8-10).

All the assays gave negative predictive values greater than 97% for pancreatic and gastric cancer (Tables 8-9) and between 72% and 82% for combined gastrointestinal cancer (Table 10). Positive predictive values were uniformly low (<14%) for pancreatic and gastric cancer (Tables 8-9), reflecting the fact that there were other cancers which gave positive results. Positive predictive values for combined gastrointestinal cancer (Table 10) were somewhat higher (22-100%). The efficiency was greater than 74% (range 74-98%) in all of the assays for both pancreatic and gastric cancer, presumably due to their high diagnostic specificities (Tables 8-9). In combined gastrointestinal cancers the efficiency ranged from 58% to 76% (Table 10). None of the assays detected the two cases of esophageal cancer.

Table 7. Comparison of Gastric Cancer Patient Results

ID#	CEA µg/L	CA 19-9 kU/L	CA 195 kU/L	CA 50 kU/L	CA 242 kU/L	CA 72-4 kU/L	Ferritin µg/L	CA 125 kU/L	CA 15-3 kU/L	CA2729 kU/L	AFP µg/L	Cyfra 21-1 µg/L	NSE µg/L
5	0.73	5.20	2.70	8.40	17.96	1.00	105.60	0.40	10.65	9.43	2.10	0.10	7.71
63	12.29	554.40	3470.00	386.00	200.00	11.40	46.84	0.00	27.72	33.95	11.92	0.60	7.75
90	20.32	505.10	8460.00	416.70	200.00	19.00	47.87	0.00	45.47	170.42	12.31	2.70	6.13
185	0.00	-	10.50	-	-	-	-	-	-	-	-	-	-
219	20.87	523.20	75.60	344.00	200.00	45.70	25.92	0.00	60.10	113.31	6.51	7.30	8.23
222	0.49	8.10	2.40	-	-	0.70	-	-	6.53	11.75	-	0.20	-
257	14.62	447.60	1164.00	313.10	200.00	2.60	353.95	125.00	29.72	37.42	2.01	0.70	8.33
278	15.75	432.10	2510.00	301.70	200.00	2.60	274.60	118.00	69.10	54.75	2.79	0.00	7.91
325	5.74	276.80	318.00	164.50	200.00	0.90	21.15	0.00	22.59	14.28	2.82	0.00	5.91
352	0.10	0.00	2.50	1.20	30.65	0.00	11.90	97.90	35.23	18.75	-	0.00	5.85
366	0.43	0.70	1.20	4.50	11.24	1.30	31.54	75.10	26.64	18.71	1.23	0.00	5.73
498	3.95	313.90	425.00	171.80	200.00	2.50	10.75	28.00	51.19	7.78	1.60	3.50	6.69
Cutoffs	5.00	37.00	10.50	25.00	69.00	5.60	M/F 250.00/ 120.00	35.00	35.00	37.70	8.90	4.80	15.00

Table 8. Comparison of Predictive Values of CEA, CA 19-9, CA 195, CA 50, CA 242, CA 72-4, Ferritin, CA 125, CA 15-3, CA 27.29, AFP, Cyfra 21-1, and NSE for Pancreatic Cancer

Marker	Sensitivity %	Specificity %	Predictive Value (+) %	Predictive Value (-) %	Efficiency %	Cutoff Value
CEA (n = 554)	37.5	79.9	5.3	97.7	78.7	5.0 µg/L
CA 19-9 (n = 541)	66.7	87.5	13.2	98.9	86.8	37.0 kU/L
CA 195 (n = 554)	100.0	76.6	11.3	100.0	77.3	10.5 kU/L
CA 50 (n = 515)	66.7	84.8	11.6	98.8	84.3	25.0 kU/L
CA 242 (n = 476)	66.7	85.0	12.7	98.7	84.4	69.0 kU/L
CA 72-4 (n = 550)	31.3	90.6	9.1	97.8	88.9	5.6 kU/L
Ferritin (n=459)	50.0	75.4	5.7	98.2	74.7	Male/Female 250.0 µg/L 120.0 µg/L
CA 125 (n = 527)	40.0	91.4	12.0	98.1	89.9	35.0 kU/L
CA 15-3 (n = 515)	26.7	75.9	3.3	97.1	74.4	35.0 kU/L
CA 27.29 (n = 494)	40.0	81.6	6.4	97.8	80.4	37.7 kU/L
AFP (n = 418)	18.2	86.9	3.4	97.7	85.2	8.9 µg/L
Cyfra 21-1 (n = 516)	26.7	95.0	13.8	97.7	93.0	4.8 µg/L
NSE (n=514)	0.0	99.8	0.0	97.7	97.5	15.0 µg/L

Table 9. Comparison of Predictive Values of CEA, CA 19-9, CA 195, CA 50, CA 242, CA 72-4, Ferritin, CA 125, CA 15-3, CA 27.29, AFP, Cyfra 21-1, and NSE for Gastric Cancer

Marker	Sensitivity %	Specificity %	Predictive Value (+) %	Predictive Value (-) %	Efficiency %	Cutoff Value
CEA (n = 554)	50.0	80.1	5.3	98.6	79.4	5.0 µg/L
CA 19-9 (n = 541)	63.6	87.0	9.2	99.1	86.5	37.0 kU/L
CA 195 (n = 554)	58.3	75.1	4.9	98.8	74.7	10.5 kU/L
CA 50 (n = 515)	70.0	84.4	8.1	99.3	84.1	25.0 kU/L
CA 242 (n = 476)	70.0	84.6	8.9	99.2	84.2	69.0 kU/L
CA 72-4 (n = 550)	27.3	90.4	5.5	98.4	89.1	5.6 kU/L
Ferritin (n=459)	11.1	75.6	0.90	97.7	74.3	Male/Female 250.0 µg/L 120.0 µg/L
CA 125 (n = 527)	40.0	91.1	8.0	98.7	90.1	35.0 kU/L
CA 15-3 (n = 515)	45.5	75.0	3.8	98.4	74.4	35.0 kU/L
CA 27.29 (n = 494)	30.0	81.2	3.2	98.2	80.2	37.7 kU/L
AFP (n = 418)	22.2	86.9	3.4	98.2	85.7	8.9 µg/L
Cyfra 21-1 (n = 516)	9.1	94.5	3.4	97.9	92.6	4.8 µg/L
NSE (n=514)	0.0	99.8	0.0	97.9	97.7	15.0 µg/L

Table 10. Comparison of Predictive Values of CEA, CA 19-9, CA 195, CA 50, CA 242, CA 72-4, Ferritin, CA 125, CA 15-3, CA 27.29, AFP, Cyfra 21-1 and NSE for Combined Gastrointestinal Cancer

Marker	Sensitivity %	Specificity %	Predictive Value (+) %	Predictive Value (-) %	Efficiency %	Cutoff Value
CEA (n = 554)	30.4	82.7	36.8	78.2	69.6	5.0 µg/L
CA 19-9 (n = 541)	29.4	91.1	52.6	79.4	75.6	37.0 kU/L
CA 195 (n = 554)	47.5	81.7	46.5	82.3	73.1	10.5 kU/L
CA 50 (n = 515)	29.3	87.7	45.3	78.1	72.6	25.0 kU/L
CA 242 (n = 476)	26.5	87.4	45.6	74.8	70.0	69.0 kU/L
CA 72-4 (n = 550)	18.2	92.7	45.5	77.4	74.2	5.6 kU/L
Ferritin (n=459)	16.4	71.7	16.4	71.7	57.7	Male/Female 250.0 µg/L 120.0 µg/L
CA 125 (n = 527)	13.5	91.9	36.0	75.9	72.1	35.0 kU/L
CA 15-3 (n = 515)	24.1	75.8	27.1	72.8	61.7	35.0 kU/L
CA 27.29 (n = 494)	15.8	79.8	22.3	72.0	62.6	37.7 kU/L
AFP (n = 418)	11.7	86.2	23.7	72.7	66.2	8.9 µg/L
Cyfra 21-1 (n = 516)	11.9	96.6	55.2	75.8	74.6	4.8 µg/L
NSE (n=514)	0.8	100.0	100.0	73.3	73.4	15.0 µg/L

DISCUSSION

In this study, we compared thirteen serologic antigens (CEA, CA 19-9, CA 195, CA 50, CA 242, CA 72-4, ferritin, CA 125, CA 15-3, CA 27.29, AFP, Cyfra 21-1, and NSE) for their efficacy at detecting pancreatic, gastric, and combined gastrointestinal cancer. Analytical parameters compared favorably for all the assays except ferritin. Both the within-run and the between-run precisions were poor for ferritin, but all other values were below 20%. The linearity was excellent for all the assays. The minimum detectable concentration of analyte (zero calibrator/diluent mean + 2SD) was slightly higher for CA 125, ferritin, and NSE than for the other assays. These tests were therefore repeated using patient samples that had previously given a result of 0 kU/L [U/mL] (data not shown). The results did not differ from those of the zero calibrator/diluent, confirming their values. Both the minimum detectable concentration and the normal/healthy adult reference interval for CA 242 were higher than expected. The normal reference intervals were broader than those cited by the manufacturers for all the assays except CA 125, CA 72-4, CA 27.29, AFP, ferritin and NSE. The CA 19-9 assay exhibited a significantly higher reference interval for males than for females; otherwise there were no significant differences between the sexes. The assays compared favorably for cost and availability of instrumentation. With the exception of CEA, CA 242, AFP, ferritin, and NSE, all of the assays were radiolabeled (I^{125}) and therefore had shorter shelf lives. The turnaround time varied from 1 hour for AFP (automated assay) to approximately 3-24 hours for the other assays (manual assays with varying incubation periods).

In order to compare the diagnostic parameters of the thirteen tumor antigens, sera from 554 patients seen in a local hospital were assayed and their diagnostic parameters compared. The physicians' diagnoses and the manufacturers' suggested cutoff values or cutoff values derived from our normal reference interval (CA 242) and the literature (ferritin) were utilized to assign the test results to the categories of true or false positives and negatives. Predictive values were calculated for

pancreatic, gastric, and combined gastrointestinal cancer. The two most important findings of this study were the observations that: (a) CA 195 exhibited 100% diagnostic sensitivity for pancreatic cancer with values reaching 1200x ULN, and (b) CA 50 and CA 242 were clearly superior to CA 72-4 for the detection of gastric cancer, exhibiting diagnostic sensitivities of 70% as compared to 27%. The importance of the pancreatic cancer findings derives from the fact that 9/16 patients exhibited serum CA 195 levels in excess of 20x ULN, seven of these results were greater than 50x ULN and two of these exceeded 1000x ULN prior to patient diagnosis by conventional means. This leads one to wonder if the patients had been tested earlier, might they have been diagnosed sooner when their prognoses were better. The importance of the gastric cancer results stems from the fact that CA 72-4 has been reported to be the best tumor marker for gastric cancer and is currently being marketed as a gastric/gastrointestinal cancer marker. However, our test results suggest that eight other antigens (CA 50, CA 242, CA 19-9, CA 195, CEA, CA 15-3, CA 125, and CA 27.29) were superior (30-70% sensitivity) to CA 72-4 (27% sensitivity) for the detection of gastric cancer. CA 19-9, CA 195, CA 50, and CA 242 exhibited the best diagnostic sensitivities for pancreatic, gastric, and combined gastrointestinal cancers, with CEA performing nearly equivalently for gastric and combined gastrointestinal cancers. Since CA 19-9, CA 195, CA 50, and CA 242 share very similar epitopes, it should not be surprising that all four react similarly. Likewise, CEA shares some antigenic determinants with CA 19-9 (5). By contrast, the diagnostic specificities of CA 72-4, CA 125, Cyfra 21-1, and NSE were superior to those of the other markers for all of the different gastrointestinal cancers. This could be the result of the low prevalence of ovarian and uterine cancer, since three of the markers have been described in cancer of the female reproductive organs (sources for increased false positives and therefore decreased diagnostic specificity). Similarly the low prevalence of cancers of neuroendocrine origin may contribute to the high NSE specificity. The prevalence of lung cancer was also relatively low which could account for the high diagnostic specificities of Cyfra 21-1 and CEA (5, 41). While CA 15-3 has been reported in cases of gastrointestinal cancer (5), in this study it was primarily elevated in cases of breast cancer (63% sensitivity, 81% specificity, 34% PV+, 93% PV-, 78% efficiency for breast cancer). This supports its current use in therapeutic monitoring of mammary cancer patients and explains its modest sensitivity and specificity for gastrointestinal cancers. The combined use of multiple tumor markers is generally believed to increase the sensitivity and decrease the specificity of the test (5). The increased sensitivity is due to the heterogeneity of many tumors with different proportions of their cell populations, and hence of antigens shed by them, being recognized by different assays. The decreased specificity is due to the fact that each assay will give a positive test for some benign and nonmalignant diseases and the use of multiple assays increases the likelihood of detecting elevations of at least one marker in a specimen. Our study results did not support the use of multiple markers for either pancreatic or gastric cancer (data not shown). It should also be noted that there is always the possibility that patients classified as "without disease" may have as yet undiagnosed subclinical disease (cancer). It is conceivable that in the future the use of ratios of multiple tumor markers may allow one to detect a very early cancer and to better discriminate its source. If that should prove to be the case, then it may justify the additional cost of multiple testing.

The findings of this study with respect to pancreatic cancer markers are supported by the work of Andicoechea et al., who found CA 195 to be superior to CEA for the diagnosis of pancreatic carcinoma (42). In similar studies, Banfi et al (43) and Giulianotti et al (44) reported that CA 19-9 and CA 195 had equivalent diagnostic sensitivities and these were considerably greater than those for CEA. Banfi also reported that CA 242 had a lower sensitivity but higher specificity than CA 19-9 and CA 195. Masson et al (45) reported diagnostic sensitivities and specificities in excess of 80% for CA 19-9, CA 50, and CA 195, whereas CEA had low specificity when using cutoffs that gave comparable sensitivity. They also observed significant differences in the CA 50 levels detected by two different analytical methods (IRMA vs DELPHIA) using the same monoclonal antibody. In a study by Oremek et al (46), the diagnosic sensitivities of CA 19-9 (68%), CA 50 (63%), CA 72-4 (49%) were superior to CEA (37%) but inferior to a pyruvate kinase-type tumor M2 marker. By contrast, Sagar et al (47) found that both CEA and CA 195 detected pancreatic cancer and the recurrence of disease following surgery. They reported that in patients with metastatic pancreatic cancer, the CA 195 was significantly higher but did not discriminate between operable and inoperable disease.

For the diagnosis of gastric cancer, Pectasides et al. (48) found CA 50 and CA 19-9 to be superior to CEA. In a similar study, Haglund et al. investigated CA 19-9 and

CA 50 for their diagnostic capabilities and found them to have the same sensitivity for gastric cancer (49). In two other studies, the authors reported a discrepancy between the markers depending on the stage of the cancer. In a study involving 100 cancer patients, Kodama et al. (50) reported that in advanced cancer CA 72-4 was superior to CEA and CA 19-9 for the diagnosis, prognosis, and detection of recurrent disease. By contrast, they found CA 19-9 and CEA to be better for the detection of early stage (I and II) disease. Likewise, in a study by Van-Dalen and Kessler (51) in which serum samples from 23 labs were analyzed for CEA, CA 15-3, CA 19-9, CA 72-4, CA 125, Cyfra 21-1, and AFP, the authors reported that CA 72-4 was the most sensitive for stage IV disease. However, the authors found CA 72-4, CA 19-9, and CEA to be equally sensitive for stage I-III disease. By contrast, in a study of 242 patients by Spila et al. (52), the authors found that CA 72-4 was superior to both CEA and CA 19-9 for the diagnosis and prognosis of both primary and recurrent gastric cancer. Likewise, Fernandez-Fernandez et al. have reported that in a study of 167 patients with gastric cancer and 92 patients with benign disease, they found CA 72-4 to be superior to both CA 19-9 and CEA at all stages of disease (53). Discrepancies between their results and ours could be the result of genetic differences in the patient populations, the stage of the tumors, the presence of pathologic complications and/or the use and type(s) of therapies.

CONCLUSIONS

In conclusion, thirteen assays (CEA, CA 19-9, CA 195, CA 50, CA 242, CA 72-4, ferritin, CA 125, CA 15-3, CA 27.29, AFP, Cyfra 21-1and NSE) were evaluated for their efficacy at diagnosing pancreatic, gastric, and combined gastrointestinal cancer. CA 195, CA 19-9, CA 50, and CA 242 were superior to the other assays for the detection of pancreatic cancer, but only CA 195 detected all of the cases. Likewise, CA 50 and CA 242 proved to be superior to the other assays for gastric cancer with CA 19-9, and CA 195, also proving effective. In contrast to previous studies, our results did not support the use of CA 72-4 for the diagnosis of gastric cancer. None of the assays detected the two cases of esophageal cancer, and none were particularly sensitive for combined gastrointestinal cancer or for colorectal cancer, which constituted the bulk (101/144) of the gastrointestinal cases in our patient population.

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Starburst Quaternary Ammonium Salt: A New Effective Phase Transfer Catalyst

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Abstract: 3,5-Bis [(2-methyl-naphthylene-1-yl) - phenyl-amino-phenyl] – butyl - (2-methoxy-naphthalene-1-yl) – phenylammoniumbromide (BPBPB) was synthesized and it was characterized using various instrumental techniques. The application of BPBPB as a Phase Transfer Catalyst (PTC) is studied by utilizing common organic reactions. The result of the PTC application of BPBPB was compared with Butyldimethylanilinium bromide BDAB (synthesized) and Tetrabutylammonium bromide (available) TBAB. Of the three, BPBPB is an efficient catalyst for certain organic reactions, and both the synthesized PTCs are regenerative to about 95% in weight.

Key Words: Phase Transfer Catalyst, starburst compounds, heterogeneous system.

INTRODUCTION

Phase transfer catalysis has emerged as a useful green chemistry technique for carrying out organic synthesis with ease and economical viability. Phase transfer catalysts help the reactants in different phases to come together and react with each other, often with catalytic efficiency under milder conditions that can be easily devised. Since its discovery, phase transfer catalysis has been in use for more than three decades and is an established technique nowadays in organic synthesis [1].

In a heterogeneous system of two immiscible solvents, reaction between the reactants contained in them is very slow due to the lack of effective interaction. This problem can be solved using organic solvents such as ethanol, dioxane, acetone, etc. But the difficulty has been that most of the inorganic salts are less soluble in these solvents; moreover, some of these solvents are toxic. The problem was remedied, at least in part by the utilization of dipolar aprotic solvents like dimethylsulfoxide, dimethylformaamide, or hexaethylphosphorictriamide. These solvents are toxic, expensive, and are difficult to remove after the reaction. These problems can easily be solved in many cases by the use of the technique of Phase Transfer Catalysis (PTC). This technique was aptly used by Starks [2], and within a short period of time it became an active subject of research with deep implications, especially in preparative organic, organometallic, and polymer chemistry. Phase transfer catalysts are substances which transfer a reactant, from the aqueous phase where the inorganic reactants are normally soluble, across the inter-phase boundary in a two-phase heterogeneous aqueous–organic solvent system, and the phenomenon continues so as to affect the progress of the reaction. These catalysts are used in very small amounts and can perform the important function of transporting the reactant repeatedly into the appropriate phase. A large number of structurally different phase transfer catalysts are currently available. Some of the common catalysts include quaternary ammonium and phosphonium compounds [3], crown ethers [4] and linear ethers [5].

The main class of phase transfer catalysts is crown ethers [6]. These are expensive and toxic in nature. The compounds consisting of quaternary ammonium, phosphonium, arsonium, etc. have also been found to be effective as phase transfer catalysts. These compounds must satisfy at least two fundamental conditions in order to function as phase transfer catalysts (i.e., their solubility in organic phase and absence of steric hindrance around the cationic center to function as an effective cation–anion pair). The types of quaternary ions found to be most

effective are those with four relatively large alkyl or aryl substituents on nitrogen, rather than with one particularly long alkyl or aryl chain [7]. A PTC works by encapsulating the ion. The PTC–ion system has a hydrophilic interior containing the ion and a hydrophobic exterior.

This paper mainly highlights the synthesis of quaternary ammonium ion with starburst substituents. Starburst compounds are star-shaped, high molecular weight compounds. Quaternary ammonium salts having a structure similar to starburst compounds have already been reported to show excellent catalytic activity [8, 9]. Because of this we have quaternarised a starburst tertiary amine that is then converted to a quaternary ammonium salt, which may act as a good phase transfer catalyst. Also, the starburst tertiary amine compound that we synthesized showed properties such as high organophilicity, large lipophilicity and high electron capturing capacity, which are the most important criteria for a phase transfer catalyst. These substituents are decidedly organic and therefore likely to be soluble in non-polar organic solvents, despite the presence of the positively-charged nitrogen and negatively-charged counter ion. At the same time, the ionic nature of the ammonium ion renders them soluble in aqueous media. This makes them move back and forth between the two phases [10].

By using a phase transfer catalytic process, one can achieve faster reactions, obtain higher conversions or yields, make fewer byproducts, eliminate the need for expensive or dangerous solvents which dissolve all the reactant in a single phase, eliminate the need for expensive raw materials and minimize waste problems. Phase transfer catalysts are especially useful in green chemistry by allowing the use of water and reducing the need for organic solvents [11-13].

The objective of this paper is also to compare the catalytic effects of a known PTC with two synthesized ones, viz; Tetrabutylammonium bromide (known) with Butyldimethylanilinium bromide and 3,5-bis[(2-methyl-naphthylene-1-yl)-phenylamino-phenyl]-butyl-(2-methoxy-naphthalene-1-yl)-phenylammoniumbromide (synthesized) using certain organic reactions.

EXPERIMENTAL

2.1. MATERIALS

The reagents [2-Naphthol, aniline, N,N-dimethylaniline, Mohr's salt (Merck, India), 1-Bromobutane, CuCl, Bromobenzene, (Loba Chemie, India), 2-Methoxynaphthalene, Tetrabutylammoniumbromide (TBAB) (SRL India), K2CO3 (NICE chemicals), KI (Qualigens, India)] are purified before use as per common laboratory procedure [14,15]. Silica Gel (60-120 mesh, SRL, India) and Bromine (Merck) are used as such. The solvents were distilled before use according to procedures available in literature [14,15]. Spectroscopic grade solvents (Merck, India) were used for UV-Vis analysis.

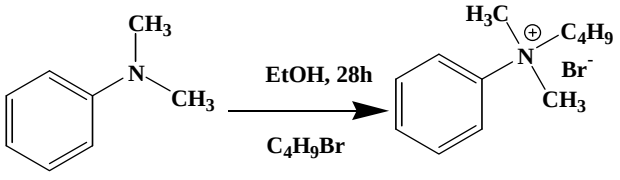
Melting points were determined in open capillaries using melting point apparatus (JSGW, Gujarat) and are uncorrected. FT-IR spectra were recorded on a Schmidzu 8400 S; UV-Visible spectra were recorded on a UV-Vis. Schmidzu 1700 using 1cm length quartz tube; 1H NMR spectra were recorded on a NMR-JEOL GSX-400 with CDCl3 as solvent.

2.2. METHODS

2.2.1. Preparation of Butyldimethylanilinium bromide (BDAB)

N,N-dimethylaniline (0.014mol, 1.76ml) in dry ethanol (25ml) was mixed with 1-bromobutane (0.02mol, 2.17ml). The contents were refluxed for 28 hours with constant stirring. The completion of the reaction was checked by TLC. The solvent was distilled under vacuum and the oily residue was purified using column chromatography. The crude product, BDAB, was washed with ether and allowed to dry. A dark blue, oily liquid was obtained [16].

Boiling point:
145°C; Yield 50.7%; UV-Vis (Ethanol, nm) 357, 341;
IR (KBr, υ cm^{-1}):
3419(NH^+), 3026, 2962 (Ar-H), 1310 (C-N);
NMR ($CDCl_3$, δ):
0.96-3.24 [9H, butyl], 3.72 [6H, methyl], 7.57-7.95 [5H, Ar].



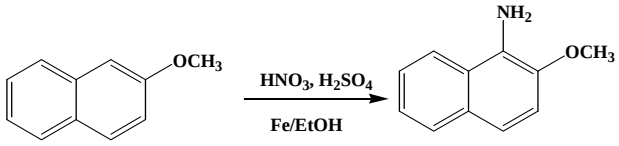
Scheme 1: Synthesis of Butyldimethylanilinium bromide (BDAB)

2.2.2. Synthesis of 3, 5-bis [(2-methyl-naphthylene-1-yl)-phenylamino-phenyl]-butyl-(2-methoxy-naphthalene-1-yl)-phenylammoniumbromide

2.2.2.1. Synthesis of Methoxy naphthyl amine

5ml Conc. H2SO4 was added drop wise to 2-methoxy naphthalene (0.01mol, 1.58g) at such a rate that the temperature does not exceed 5oC. To this, 4 ml Conc. HNO3 was added drop wise with stirring at 0oC. The mixture was stirred at 0oC for an hour, at room temperature and at 55oC for another hour, filtered and dried. It was then refluxed with Mohr's salt (1.5g) for one hour. The contents were allowed to cool and then filtered and washed with ethanol [17].

Yield 75.1%; Melting point: 72oC;
IR (KBr, υ cm-1):
3467, 3379 (-NH2), 3083, 3029 (Ar-H), 2842, 1434 (-OCH3), 1218 (C-O-C), 1250 (C-N);
NMR (CDCl3, δ):
3.9 (6H, -OCH3), 4.0 (2H, -NH2), 7.31-7.44 (6H, Ar).

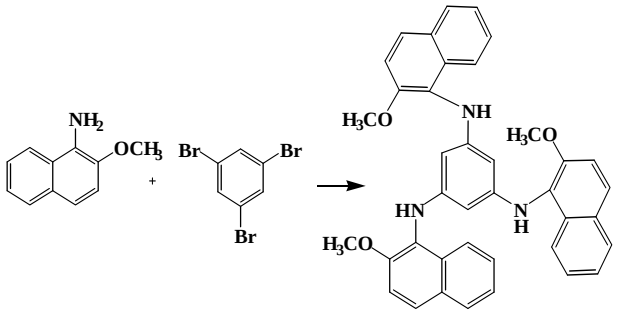


Scheme 2: Synthesis of Methoxy naphthyl amine

2.2.2.2. Synthesis of N,N,N′-Tris-(1-methoxynaphthalen-2-yl)-benzene-1,3,5-triamine

1-Amino-2-methoxy naphthalene (0.03mol, 5.67g), tribromobenzene (0.01mol, 3.30g), CuCl (200mg), K2CO3 (1.0g) and KI (1.0g) were refluxed in acetone (20ml) for 10 hours at 60oC. After the completion of the reaction (checked by TLC), it was extracted using ether. Solvent was removed by vacuum distillation and the product was recrystallised from ethanol [18].

Yield: 40.5%; Melting point: 50°C;
IR (KBr,ν, cm-1):
3429 (N-H), 3071, 2950 (Ar-H), 2843, 1435 (-OCH_3), 1218 (C-O-C), 1250 (C-N);
NMR ($CDCl_3$, δ):
3.9 (9H, -OCH_3), 4.0 (3H, NH), 7.1-8.7(21H, Ar).

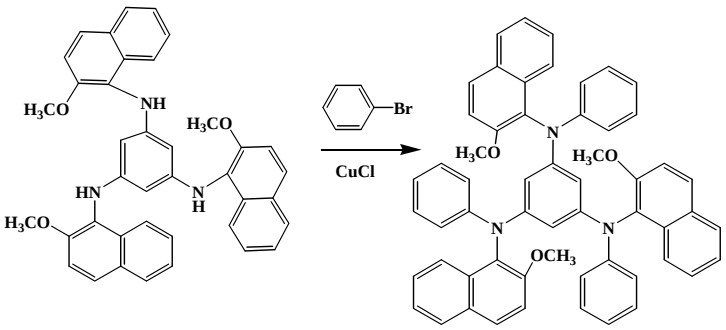


Scheme 3: Synthesis of N,N,N′-Tris-(1-methoxynaphthalen-2-yl)-benzene-1,3,5-triamine

2.2.2.3. Synthesis of N,N,N`-Tris-(2-methoxy-naphthalenen-1-yl)-N,N,N′-triphenylbenzene-1,3,5-triamine

N,N,N`-Tris-(2-methoxy-naphthalenen-1-yl)-N,N,N`-triphenylbenzene-1,3,5-triamine (4.2g, 0.0071mol) and bromobenzene (0.0213mol, 2.2ml) are coupled using Copper (200mg) catalyst in basic medium by refluxing the contents for 10hour at 60oC [19].

Yield: 38.5%; Melting point: 47oC;
UV-Vis. (Ethanol, nm) 358, 364, 286;
IR (KBr,υ, cm-1):
3084, 2981 (Ar-H) 2842, 1435 (-OCH3), 1219 (C-O-C), 1259 (C-N);
NMR (CDCl3, δ):
3.97(-OCH3), 7.19-8.7 (36H, Ar).

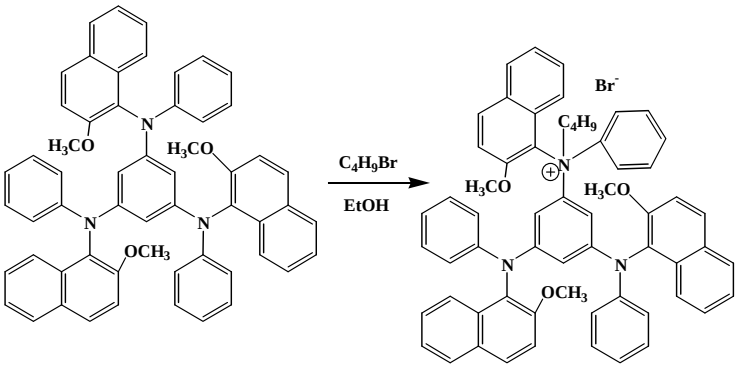


Scheme 4: Synthesis of N,N,N`-Tris-(2-methoxy-naphthalenen-1-yl)-N,N,N′-triphenylbenzene-1,3,5-triamine

2.2.2.4. Synthesis of 3, 5-bis[(2-methyl-naphthylene-1-yl)-phenylamino-phenyl]-butyl-(2-methoxy-naphthalene-1-yl)-phenylammonium bromide (BPBPB)

The compound was synthesized as per the same procedure adopted for the synthesis of BDAB [16].

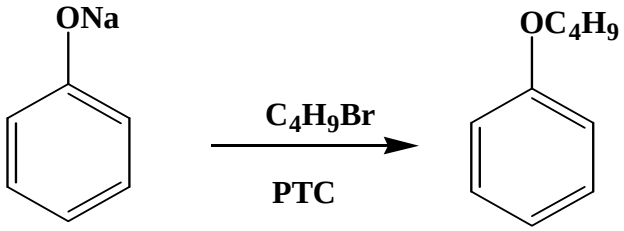
Appearance: Yellow solid;
Yield: 45.1%; UV-Vis (Ethanol, nm) 358, 364, 391;
IR (KBr, υ cm^{-1}):
3343 (NH^+), 3074, 2940 (Ar-H), 2843, 1435 (-OCH_3), 1218 (C-O-C), 1259 (C-N);
NMR ($CDCl_3$, δ):
0.96-3.33 (9H, Butyl), 3.95 (9H, -OCH_3), 7.01-8.2 (36H, Ar).



Scheme 5: Synthesis of 3, 5-bis[(2-methyl-naphthylene-1-yl)-phenylamino-phenyl]-butyl-(2-methoxy-naphthalene-1-yl)-phenylammonium bromide (BPBPB)

RESULTS & DISCUSSION

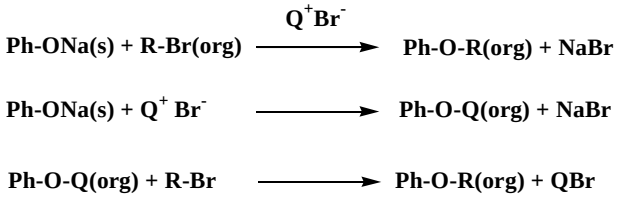
Quaternary ammonium compounds are widely used industrially and commercially [20]. Owing to their extensive use, exact and simple conditions for their preparation should be summarized. Two types of phase transfer catalysts are synthesized as given in the experimental part and their activity is compared with a commercially available catalyst. Catalytic activity of TBAB, BDAB and BPBPB were tested for the substitution reaction between sodium phenolate and N-butyl bromide. Typical experiments were conducted by mixing 0.03mol of n-butyl bromide in toluene (25ml) and 0.03mol of sodium phenolate in water (20ml) and a suitable quantity of PTCs (0.003mol) at 70oC for 4.0 hours [21].



Scheme 6: Synthesis of phenylbutylether

PTCs are usually used in heterogeneous immiscible liquid phases that are in contact with an aqueous phase containing an ionic reactant and an organic phase containing the organic substrate. Normally the reaction of two substances in separate phases is inhibited because of the inability of the reagent to come together. Adding a PTC solves this problem by transferring ionic reactant into the organic phases. Because the reaction medium is aprotic, an SN2 reaction occurs rapidly [6].

Formation of phenyl butyl ether using PTC follows the below mechanism.



Q+Br- is the PTC, where Q+ (Quaternary ammonium ion) is the lipophilic center, which can move back and forth between the two phases. As the ammonium ion moves from the aqueous phase into the organic phase, it carries with it negatively charged 'PhO-' ion. If it travels as the part of an ammonium ion pair, the phenoxide ion can be transported from the aqueous phase into the organic phase in which it is ordinarily insoluble. The phenoxide ion is greatly stabilized through solvation in the polar environment in which it is dissolved. When it is transported into the organic layer, it arrives bare -- shorn of its solvating and stabilizing water molecules. Therefore, it is in a highly reactive state. Unsolvated phenoxide is far more reactive than solvated phenoxide. Under these conditions, formation of phenylbutylether is quantitative and complete in 4 hours.

We use three PTCs to carry out the reactions at different conditions (i.e., by changing the concentration of the catalyst). The results are given in Table 1 and shown in Figure 1. From the Table, it can be concluded that BPBPB gives the maximum yield at an optimum concentration of 0.001mol. The reactivity sequence of the

three PTCs is as follows: BPBPB > TBAB > BDAB. The different reactivity for catalysts is due to the lipophilic property of cation group in catalyst which governs the formation of catalytic intermediate.

Table 1: Yield of ether at various concentrations of TBAB, BDAB and Starburst PTC

Sl. No	TBAB		BDAB		Starburst PTC (BPBPB)	
	Conc. molx10^{-4}	Yield %	Conc. molx10^{-4}	Yield %	Conc. molx10^{-4}	Yield %
1	5.0	45.2	5.0	41.4	5.0	57.0
2	10	48.0	10	43.0	10	60.8
3	20	50.0	20	45.3	20	58.0
4	30	53.5	30	50.0	30	55.6
5	40	52.0	40	48.0	40	50.0

Sodium phenoxide: 0.03mol; Butyl Bromide: 0.03mol; Toluene 25cm3; Temperature: 70oC Time: 4Hr.

CONCLUSIONS

Of the three PTCs, BPBPB is efficient for the formation of Phenylbutylether. It is observed that BDAB and starburst PTC are regenerated up to 95% by weight, but TBAB is not regenerated.

The catalytic activity of starburst PTC (BPBPB) is almost similar to that of heterogeneous PTC [21, 22]. (See Table 1 for concentration and yield comparison.)

The efficiency of starburst PTC is due to the following factors: 1) high molecular weight of aryl group and large organophilicity, 2) lipophilic property of cation group in catalyst due to the presence of same type of aryl group on nitrogen [23].

Due to the above factors, starburst PTC is efficient not only for esterification, but also for many other organic reactions. This PTC is having a wide range of industrial application. Further studies are being conducted on the synthesis of various types of starburst PTC and their utilization in various other organic reactions.

NOMENCLATURE

TBAB - Tetrabutylammonimbromide
BDAB - Butyldimethylanilinium bromide
BPBPB - 3,5-Bis[(2-methyl-naphthylene-1-yl)-phenylamino-phenyl]-butyl-(2-methoxy-naphthalene-1-yl)-phenylammonium bromide.

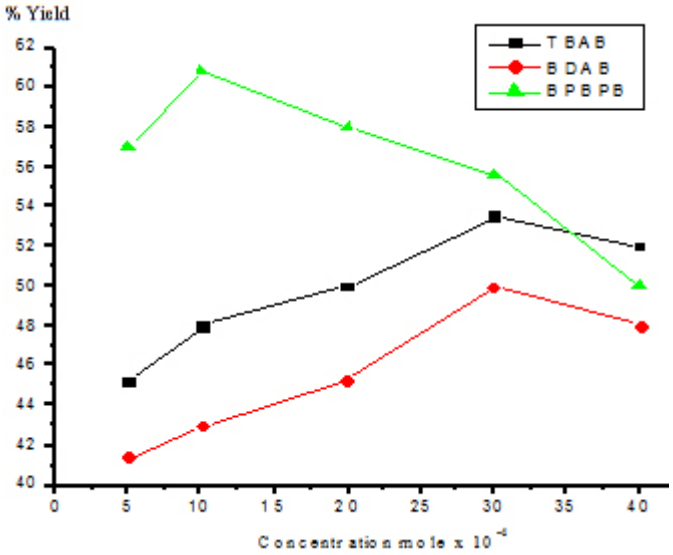


Figure 1: Variation of % yield with concentration of PTCs

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The Combustion of Denatured Alcohol and Its Role in a Legal Case

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Abstract: On a warm spring day in Howell, MI, April 30, 2010, the Victim pulled into her driveway and was accosted by the Defendant. He sprayed the cologne *Charlie* onto the Victim, depressing the plunger three or four times. The vapor ignited resulting in a flame that surprised both the Victim and the Defendant. The Defendant was taken into custody and charged with Assault with Intent to Murder. The physical properties of the cologne in combination with weather conditions that day increased the likelihood that, in the presence of an ignition source, flaming combustion of the atomized vapor of the cologne could occur. The Defendant, to a reasonable degree of scientific certainty, could not have anticipated that the flammable *Charlie* product could produce visible flame under these conditions. While spraying a flammable substance upon another person is an apparent assault, the facts of this case and the application of the fundamental science do not, to a reasonable degree of scientific certainty, support the charge of Assault with Intent to Commit Murder.

Key Words: Aerosol, flash point, lower and upper explosive/flammability limits and denatured alcohol.

INTRODUCTION

On a warm spring day in Howell, MI, April 30, 2010, the Victim was driving a Volkswagen convertible with the top down when she pulled into her driveway at ca. 6:00 PM EDT. The Defendant (the Victim's ex-boyfriend) approached the vehicle and sprayed the atomized mist of cologne into the Victim's cleavage. The vapor was ignited by a spark, resulting in a flame that left both the Victim and the Defendant shaken.

Three felony counts were subsequently brought against the Defendant (Victim), including Assault with Intent to Murder. Documents provided by the Public Defender and the discussion with the Defendant indicated that he had used the commercial product *Charlie* in this incident. A typical sample of *Charlie* contains about 3.5 o.z. of spray cologne. *Charlie* is dispensed as an atomized mist when the plunger is pressed down. The dispensing of *Charlie* follows the same basic principle in dispensing the desired product contained in an aerosol can **[1]**.

DEFINITIONS & SCIENTIFIC TERMS

An **aerosol** has to two primary components: a **Product** (the desired chemical) and a **Propellant** (the agent that enables the propellant to be dispensed) **[1,2]**.

Flash Point – The minimum temperature of a gaseous fuel in the presence of an ignition source and oxygen that produces a visible flame **[3]**.

Lower and Upper Explosive/Flammability Limits – A mixture of gaseous fuel in air (under standard conditions of atmospheric pressure and temperature) is explosive/flammable when the percentage of the gaseous fuel in air is in the range between the lower and upper limits **[4]**.

Concentration – The amount of a given chemical divided by the total volume.

DISCUSSION OF FINDINGS & RESEARCH

The ingredients in *Charlie* are: **SD Alcohol 40-B, Fragrance, Water, BHA or butylated hydroxyl anisole** (a preservative)**, Benzophenone-2, D&C Orange No. 4,** and **FD&C Blue No. 1 [5]**.

When listing the ingredients in many commercial products, the order is on the basis of decreasing concentration. The SD Alcohol 40-B is present in the largest amount; the two dyes (D&C Orange No. 4 and FD&C Blue No. 1) are present in the least amount. This rationale supports the warning that *Charlie* is flammable.

The alcohol present in *Charlie* is not intended for drinking. Alcohol products of this type are designated as **denatured alcohol**. The alcohol product intended for drinking is ethyl alcohol or ethanol (C_2H_5OH). The designation SD in the list of ingredients in *Charlie* means that the alcohol has been specially denatured. The US Bureau of Alcohol, Tobacco, and Firearms designation 40-B indicates that the compound denatonium benzoate was used to denature the alcohol **[6]**.

The compound denatonium benzoate is considered to be the bitterest compound known. Other applications for this denaturing compound include: deer repellent, nail polish (to discourage nail-biting), paints, antifreeze and windshield washing fluid (to prevent accidental ingestions), and to coat electrical cables to prevent rats from eating the insulation **[7]**.

Benzophenone-2 is used as an ingredient (used) since it is an absorber of ultraviolet light. This energy is dissipated as heat **[8]**.

The primary ingredient in *Charlie* is 70% ethanol. The flash point for this concentration is 61.9°F (16.6°C). Ethanol, in the presence of an ignition source and sufficient oxygen, is flammable at a temperature less than ambient or 72°F (22°C). The respective lower and upper explosive/flammability limits are cited as 3.3% and 19.0% by volume **[9]**.

The flash point for denatured alcohol is 55°F (13°C) **[10]**. This means that ethyl alcohol not intended for drinking can have its vapor produce a visible flame, in the presence of an ignition source and oxygen, at a considerably lower temperature than ethyl alcohol intended for drinking. Per the warning on *Charlie*, we must reiterate the flammable nature of this product.

Under Handling and Storage of the MSDS for 70% ethanol, explicit comments emphasize avoiding static sparks and static electricity, plus other ignition sources.

The Weather Underground website maintains historical meteorological data. The weather data for Howell, MI at 5:55 PM EDT on April 30, 2010 is given in Table 1 **[11]**. The weather conditions identified at the approximate time of the incident are a typical breezy spring day. (This set of weather conditions is also consistent with the conditions reported at the National Weather Service station in Flint, MI.)

Table 1. Weather Data at Howell, MI for 5:55 PM EDT on April 30, 2010 [11]

Temperature = 77.0ºF
Dew Point = 53.6ºF
Relative Humidity = 44%
Barometric (Sea Level) Pressure = 29.60 inches (Hg)
Visibility = 7.0 miles
Wind Direction = South-South-West (SSW)
Wind Speed = 17.3 miles per hour
Wind Gust Speed = 24.2 miles per hour
Conditions = Clear

The Victim was driving a Volkswagen convertible with the top down when she pulled into her driveway at ca. 6:00 PM EDT. In (By) his own words (testimony), the Defendant pushed down on the *Charlie* product plunger three (3) or four (4) times. The atomized cologne mist was directed toward the Victim's cleavage when a visible flame was observed.

The ignition source, to a reasonable degree of scientific certainty, was static electricity. Contact of the Victim's clothing with the upholstered seat and her shoes with the carpet in the car was sufficient to produce flaming combustion on this warm, dry day. Typical ignition sources, such as lighters and matches, were not found.

The Defendant had been driving a black truck during the day on April 30, 2010; the *Charlie* was in the truck most of the day. It is clear from this information and the supporting weather data that the ambient temperature conditions exceeded that of the flash point for denatured alcohol (55°F = 13°C). All that was needed for the observation of flaming combustion was an ignition source.

OPINIONS

The Defendant acknowledges that he did spray the atomized mist of the commercial product *Charlie* cologne

into the Victim's cleavage on April 30, 2010 at ca. 6:00 PM EDT. The resulting flame left the Victim shaken. This event most definitely scared the Defendant.

The Defendant is neither trained in chemistry nor does he have experience in understanding the relevant key terms Flash Point and Lower and Upper Explosive/Flammability Limits.

The presence of denatured alcohol in *Charlie* demonstrates why this commercial product is flammable. The Defendant indicated that he was not aware that *Charlie* is flammable and that there are conditions that need to be avoided.

Material Safety Data Sheets (MSDS) for 70% ethanol (intended for drinking) and denatured alcohol indicate low flash point temperatures for these chemicals. The Defendant indicated that had he known the flash point for denatured alcohol is about 55°F, he would not have kept the *Charlie* in his black truck during most of this warm spring day.

The MSDS also indicate that the static sparks and static electricity are prospective ignition sources that need to be kept away from 70% ethanol (intended for drinking) and denatured alcohol. The lower flash point for denatured alcohol indicates that in the presence of an ignition source and oxygen, its vapor can produce visible flame at a lower temperature than ethanol intended for drinking.

The lower explosive/flammability limit for both 70% ethanol (intended for drinking) and denatured alcohol is 3.3% by volume in air. When *Charlie* was sprayed on the Victim and visible flame was observed, the percent of denatured alcohol had to be between 3.3% and 19.0% by volume in air in the presence of an ignition source.

The combustion leading to the visible flame was not sustained when the Defendant was no longer pushing down on the plunger. Based on the volume increase, due to the expansion of the denatured alcohol vapor around the Victim's Volkswagen convertible, the concentration of denatured alcohol vapor in air decreased to less than 3.3% and the temperature decreased to less than 55°F (13°C). As a result, the visible flame went out.

The Defendant, to a reasonable degree of scientific certainty, could not have anticipated that the flammable *Charlie* product could produce visible flame under the conditions noted here. (It is fortunate that by no longer pushing down on the plunger, the total amount of fuel was limited.)

The expansion of the denatured alcohol vapor results in increased volume (and the lower temperature). To a reasonable degree of scientific certainty, this increase in volume is sufficiently large to cause the concentration of the fuel to decrease to less than the 3.3% lower explosive/flammability limit by volume in air in the presence of an ignition source [plus the reduced temperature to less than the flash point (55°F = 13°C)] necessary for combustion.

Static electricity was, to a reasonable degree of scientific certainty, the ignition source. Neither a lighter nor matches were found. On a warm, dry day static electricity is a plausible ignition source.

Based on the information contained in the collection of documents received from the Public Defender, the Victim neither sought medical attention nor did she keep the clothes that she was wearing in this incident. As a result, these items weren't available for examination.

While spraying a flammable substance upon another person is an apparent assault, the facts of this case and the application of the fundamental science do not, to a reasonable degree of scientific certainty, support the charge of Assault with Intent to Commit Murder.

The Intent to Commit Murder specification on (portion) of the Assault charge was not included in the jury verdict.

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Challenges for Chemical Education: Implementing the `Chemistry for All' Vision

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Abstract: Over the last two decades, concern has been mounting within the chemistry profession over the general populace having negative views and opinions of chemistry, chemicals and a 'chemophobia' of chemical processes and the chemical industry. This phenomenon has been consistently blamed on the 'media' for exposing and emphasising the harmful consequences of chemical accidents and under-emphasizing or ignoring chemical triumphs. In 2004, the International Union of Pure & Applied Chemistry (IUPAC) commissioned a review of public perceptions of chemistry and sought strategies for enhancing the public image of chemistry, chemicals and the chemical industry. The subsequent report indicated the need for strategic chemical education programs dedicated to communities and embracing a 'Chemistry for All' vision to empower communities to understand the complex world in which they live. Such a program should also emphasize that the advantages and opportunities that chemistry offers to humanity in terms of enhancing global standards of living far outweigh its disadvantages and disincentives. This paper discusses the extent to which chemical education has advanced so as to develop a 'Chemistry for All' vision that can feasibly be implemented.

Key Words: Chemistry for all, chemical education, chemistry education, chemophobia.

INTRODUCTION

The perennial paradox is that, although 'chemicals' provide major recognisable benefits to humanity by raising standards of living and well-being, such benefits are largely taken for granted by the majority of the populace resulting in a prevailing negative public image of chemistry and chemicals. This is believed to be due to the global media sensationalizing environmental chemical 'incidents' whilst marginalizing erudite progress reports of major developments in science and technology and the tangible benefits of these two commodities at large [1]. This so-called 'chemophobia syndrome', which appears to be widespread in communities, is directly related to the inability of individuals to associate chemistry with materials and processes which enhance the quality of life and the quality of the natural environment which supports life. Communities need to understand that chemistry has consistently fulfilled its commitment to the needs of people, but in doing so there have been some negative spin-offs. It is unfortunate that, in general, people have consistently focussed on the latter and largely ignored the former. For example, fossil fuels currently generate the bulk of global energy requirements, but public focus tends to be concentrated on the environmental impact of the greenhouse gases that fossil fuel power generators produce.

In 2004, IUPAC commissioned an enquiry into the general public perception of chemistry and its benefits to society [1]. The subsequent report found that the prevailing widespread negative perception of chemistry correlates with limited understanding of chemistry, chemists and chemicals and an even more shallow understanding of the function and operations of the chemical industry. The report concedes that such a negative community image of chemistry can only change by concerted educational programs, promoted by organisations, such as the American Chemical Society (ACS) and the Royal Society of Chemistry (RSC), national science foundations, science policy makers, science teachers, science students and 'public forums', thereby constituting a 'Chemistry for All' educational strategy.

Most importantly, the outreach of this strategy can be enhanced by frequent blogs, YouTube videos and social media outputs from professional chemists exalting the virtues of chemistry and its active role in advancing the standard and quality of living.

This paper discusses how chemical education philosophy and pedagogy have progressively developed over the last decade to embrace the 'Chemistry for All' concept and identifies the key chemical concepts which constitute chemical literacy, leading to some understanding of how chemistry enhances standards of living whilst simultaneously enabling environmental sustainability.

THE PRESENT STATUS OF CHEMISTRY LITERACY

Since communities in general continue to have negative views and opinions about chemistry and the chemical enterprise, the present very limited level of community wide chemical literacy needs to be significantly enhanced. Initially, it is necessary to assist communities to understand and appreciate the benefits of chemistry and chemicals and its potential to enhance standards of living and sustain life. Professional chemists and chemistry educators must understand how people form their opinions about chemistry. There is abundant evidence [2, 3] to confirm that chemistry has, over many decades, created valuable materials and products which have benefited every aspect of daily living. A wide variety of consumer goods are chemically-based – cosmetics, soaps, detergents, paints and cleansing agents. Construction of modern homes employs a variety of 'chemical materials' – notably polymeric materials. Availability of high quality drinking water and processed and preserved foods involve chemical processes and agricultural development and has traditionally been dependent on chemical fertilizers and pesticides. Life expectancy has increased as a result of the development of targeted pharmaceuticals and the continued growth of the chemical industry has sustained global economies.

In view of such chemistry attributes, it is pertinent to rationalize why the general populace does not recognise the pivotal role of chemistry in not only supporting a healthy and rewarding lifestyle, but also in sustaining the environment. Unfortunately, communities only focus on the negative aspects of chemistry. Quite simply, these tend to be accentuated by adverse media coverage [4]. It cannot be denied that while chemical products have very substantially enhanced standards of living, their manufacture, use and ultimate disposal can pose varying levels of concern to people in the context of 'toxic wastes', 'water and soil contamination' and 'air pollution'. For example, the quintessential materials of the 20th century were 'polymers', which heralded the arrival of the 'plastic age' whilst simultaneously causing a most serious threat to global environmental sustainability. This phenomenon was recently brought into public focus by the voyage of 'Plastiki' across 8000 miles of the Pacific Ocean from San Francisco to Sydney [5]. 'Plastiki' was a catamaran constructed from some 12,500 discarded plastic soft-drink bottles glued together using a sugar/cashew nut (bio-degradable) mixture. The aim of the mission was to emphasise the extreme levels of 'plastic pollution' in the oceans, which cause serious reductions of marine life and degradation of marine ecosystems.

Likewise, communities are well aware of the harm caused by 'drugs of dependence', such as heroin, which destroy human lives; however, they are at the same time unaware that morphine, which is widely used to relieve pain, is closely related chemically to heroin. It is this lack of association of 'drugs' with beneficial chemical activity which in part sustains the negative opinion of 'chemistry syndrome'. Also, communities are well aware of chemicals that are used in warfare, such as Agent Orange, and especially since recent wars have been associated with 'weapons of mass-destruction'. Also, communities are concerned and sceptical about the progressive genetic modification of plant and animal species, aligning this frontier science with 'chemical-infested foodstuffs'. Hence the general populace has difficulty coping with the ethical directions in which modern chemistry is advancing, and these concerns overwhelm any positive perceptions of chemistry which are self-evident to those who are chemically literate.

Unfortunately, evidence is rapidly accumulating to suggest that the global environment is in a state of decline and public awareness campaigns are omnipresent. However, amid all the hype, the fundamental cause of this decline is often overlooked – namely that the rapidly increasing global population cannot be sustained by diminishing global resources, disproportionately consumed, and hence communities are not aware that they are largely responsible for their own ultimate demise through malnutrition. In this context, communities are not aware that chemistry can and is making major contributions to sustaining human life in areas such as food security, clean water supplies, energy security and mitigating global warming [6].

Compounding the negative image problem is that communities are unaware of what professional chemists 'do' and the difference between a 'chemist' and a 'pharmacist'. Furthermore, their image of the chemical industry is largely based on its production of the 'odours', 'colours', 'tastes' and 'textures' of everyday experience with the prefix of 'nasty' attached, and their 'chemophobia' develops from and is sustained by chemical industrial accidents which are vigorously reported in the media.

Communities blame the chemical industry for producing toxic chemicals, such as pesticides, and toxic wastes, such as 'trace metals', but they are unaware that over the last decade, the chemical industry has undergone a major restructure embracing the principles and practices of 'green chemistry', thereby forming the foundation of a sustainable chemical industry. This revolution in 'chemical practice' is further evidence of chemistry and the chemical industry making a continuing commitment to recognise and address its responsibilities to society at large.

The general populace has a fear of chemistry because it does not understand its language or the models that are used to visualise it. It can only relate to the real world and so has inordinate difficulty in relating to the microscopic world of atoms and molecules which make up the real world. Since chemistry is the science of atoms and molecules and how these interact to form the real world, the 'Chemistry for All' vision must provide educational pathways for communities to understand the microscopic world and thereby empower them to understand the macroscopic world in which they live. Furthermore, inclusion of both positive and negative attributes of chemistry in chemistry curricula in schools can also assist in resolving the image identity problem (particularly if the negative attributes of chemistry are portrayed as careless application of chemical principles and practices), and that more socially responsible (green) application of these principles can ultimately resolve these problems.

It therefore follows that community chemistry literacy is primarily empowered by strategically-structured chemical education programs which are focussed on basic chemical principles, chemical processes with emphasis on the chemical products that enhance standards of living, and chemical processes that sustain the environment.

THE PRESENT STATUS OF CHEMISTRY EDUCATION

The 'Science for All' vision is not a new phenomenon. In 1938, Hogben [7] published his classic treatise 'Science for the Citizen' with the Foreword:

> *'Science for the Citizen is partly written for the large and growing number of intelligent adults who realize that the impact of science on society is now the focus of genuinely constructive social effort. It is also written for the growing number of adolescents who realise that they will be the first victims of the new destructive powers of science misapplied.'*

This message largely remained dormant until the mid - 1980's when Fensham [8] proposed that everybody should, through progressive education, be aware of the scientific principles that affect their everyday lives. Scientific literacy is, in Fensham's view, of equal importance to reading, writing and math skills and that these four interrelated skills should be afforded equivalent prominence in the educational process of society at large. Hence, scientific literacy should be a major goal of the educational system at all levels in addition to the basic '3R's' goals. However, this creates a dilemma for educationalists since science teaching methodologies have to be developed that not only include basic science principles, but also show how these principles enhance quality of life and sustain the environment. In this context, Cross [9] argues that there is an intuitive link between a sustainable future for humanity and the impact of science on the populace; and hence the need for a 'social construction of science'. He believes that it is possible for 'ordinary people' to have a basic understanding of science so that they can interact constructively with the current debates on issues such as 'global warming', 'renewable energy resources', 'nuclear energy' and 'genetic modification of foodstuffs'. The challenge is to restructure science education so that it leads to unilateral scientific literacy and includes the evaluation of current social issues that have scientific content and focus. Such a framework better prepares people to evaluate evidence and make judgements that empower them to face the many challenges that threaten human life and the sustainability of the environment.

Embedding the 'human element' into chemistry education has been a slow process and has only recently gathered momentum following the 2006 IUPAC report [1] on the desperate need to inform and engage communities with basic chemical knowledge to allow them to make informed judgements on how chemistry (and chemicals) benefit communities. In this context Mahaffy [10] has shown that there is an integral connection between 'chemical reactivity' and 'human activity' and has proposed that the traditional three levels of learning chemistry – 'macroscopic', 'symbolic' and 'molecular' – be extended to a fourth dimension, the 'human element', leading to the so-called 'tetrahedral chemical education model'. It is this fourth dimension which has been largely overlooked in chemical education teaching and research, and a lack of relating chemistry and chemicals to the human element may have been a major factor in contributing to the negative public image of chemistry. However, inclusion of the human element leads to a new vision for chemical education which is, in principle, wider in implementation than in traditional school and tertiary education forums.

This new vision for chemical education should be closely aligned with the roadmap for the future development of chemistry, as incorporated in the United Nations charter on the International Year of Chemistry (IYC) announced in 2011 [11]. This charter identified current global crises: water quality, food security, energy security, disease control, climate change and environmental sustainability. All of these issues relate to human sustainability and chemistry enables solutions to be found [6]. However, it has been proposed by Hill and Mustafa [12] that environmental sustainability is the primary global challenge which fundamentally encapsulates all of the other IYC issues, since all are related to it. Thus, we propose that the 'new chemical education' has three dimensions, as shown in Figure 1.

Over the last two decades, there have been some notable developments of these dimensions. For example, Atkins [13] has proposed that 'chemistry is based on just a few simple ideas', which has led to re-evaluation of the content and context of secondary college and tertiary courses in 'basic chemistry', together with more effective learning processes and outcomes. Hill [14] has suggested that the Atkins philosophy correlates directly with the core chemistry knowledge of new chemical education. Also, Hill [15] has designed a curriculum framework for the tertiary 'basic chemistry' course which embraces the Atkins 'simple ideas' philosophy [13], the Fensham, and Kumar and Chubin 'Science for All' philosophy [8, 24, 25] and the Mahaffy 'human element' proposal [10]. Furthermore, Hill and Warren [16] have shown that this curriculum framework can be extended and adapted to include the 'environmental sustainability' dimension of new chemical education, thereby becoming consistent with the IYC challenges. This restructured basic chemistry course with emphasis on 'people engagement' may play a major role in reversing the lingering negative views and opinions of chemistry, chemicals and the chemical industry held by communities.

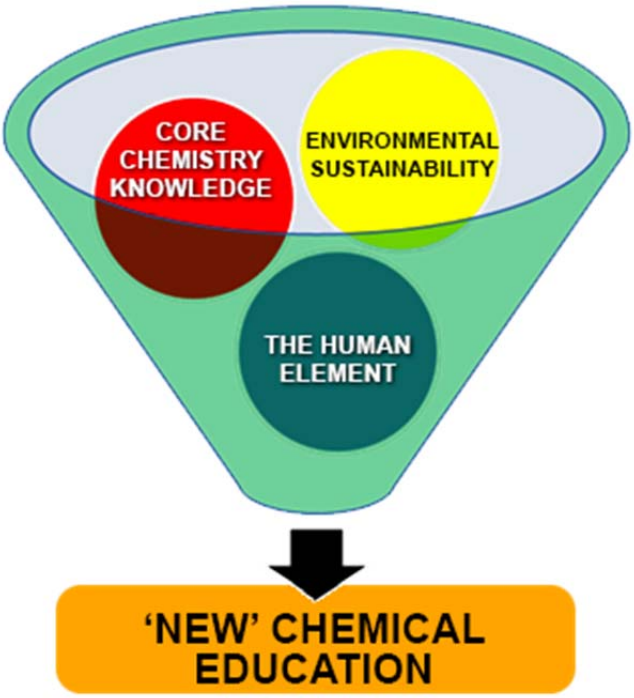

Figure 1. Dimensions of 'New Chemical Education'

TESTING THE EFFECTIVENESS OF THE NEW CHEMICAL EDUCATION PARADIGM

Climate change is probably one of the most contested contemporary issues. The pro-lobbyists argue that the scientific evidence for climate change is irrefutable [17]. The opponents and sceptics argue that such evidence is inconclusive and ambiguous and that even the term 'climate change' is ambiguous because in reality, 'climate' is 'perpetually changing' and that periods of global warming and global cooling are cyclical and have occurred before the advent of anthropogenic carbon dioxide emissions [18]. It is clear that understanding the climate change (global warming) phenomenon requires knowledge of the basic principles

of several sciences and how to mitigate it needs recognition of the associated 'social', 'political' and 'economic' aspects. Thus, science education at all levels must be intensified if the wider community, politicians and economists are to effectively address the causes and (already apparent) consequences of global warming and thereby promote a sustainable future for humanity [19]. Chemical education has a major role in the challenging process of informing the general populace of the causes of global warming using simple, basic chemical terminology and discussing options presently available for addressing it. We suggest a framework for such a community chemical education initiative on global warming, as shown in Figure 2.

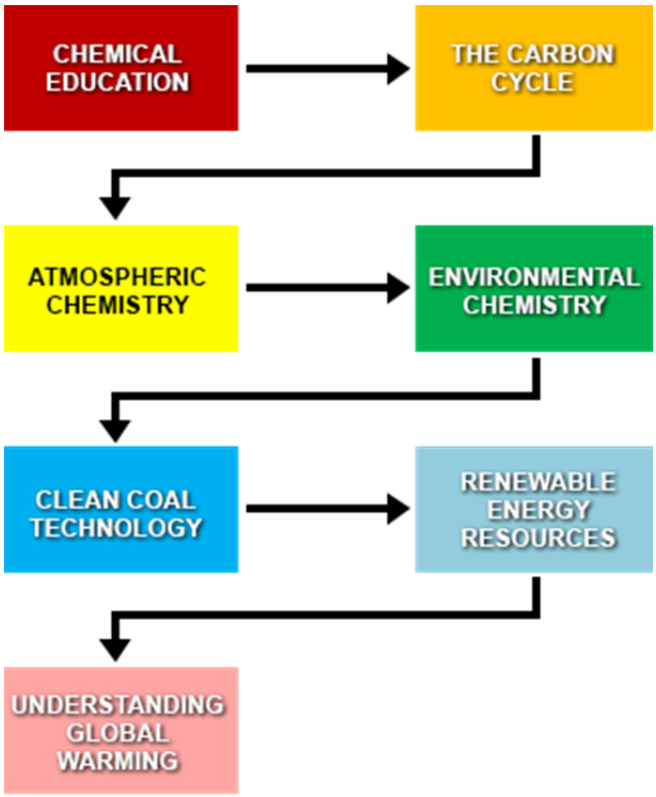

Figure 2. Understanding 'Global Warming' via Chemical Education.

Such an initiative is probably the ultimate challenge for new chemical education since topics such as 'what constitutes climate', 'what is a greenhouse gas', 'what is global warming', 'what is a renewable energy resource' and 'what is clean coal technology' have to be explained in terms that non-scientifically orientated communities can understand [20 – 23, 26]. Even more challenging is to change the 'quick fix' syndrome of the 'save the earth' organisations who argue that the only way to address global warming is to shut down the worst industrial offenders of greenhouse gas emissions, namely coal-fired power generators. In the State of Victoria (Australia), about 85% of electricity demand is provided by (brown) coal-fired power generators located in the La Trobe Valley. Peak demand is met by supplementary power provided from the Snowy hydroelectric scheme located in New South Wales. This scenario is a global phenomenon, namely that base-load electricity is predominantly provided by coal-fired power generators. The fundamental dilemma is that at present demand rates, the energy outputs of all existing energy resources (hydro, solar and wind) combined cannot provide base-load power requirements and hence closure of coal-fired power generators will cause catastrophic and unmanageable reductions in global power generation. The logical (compromise) solution is to 'clean' existing coal-fired power generators by application of clean coal technology (CCT). However, a further dilemma is apparent in that CCT in its various manifestations is at an 'experimental stage' and is not expected to become commercially available for at least a decade. Thus, a carefully constructed chemical education program is able to provide the general populace with a balanced interpretation of the global warming phenomenon, its causes, consequences and its credible mitigation strategies.

Finally, a public chemical education program can include an introduction to the intangible concept of environmental sustainability by giving meaning to the jargon of global warming, such as 'carbon tax', 'carbon economy', 'carbon footprint', 'energy crisis', 'green energy' and 'carbon emission trading scheme', all of which are currently widely used in the media, but usually with inadequate explanation. Such programs are likely to have widespread public appeal, particularly if delivered via the unsurpassed outreach capacity of the internet by way of Facebook, YouTube, blogs and perhaps Skype. These online chemical education initiatives should involve professional chemists and chemical educators interactively discussing contemporary chemical phenomena in terms which the general public can relate to and understand. Commercial sponsorship can probably be obtained to fund such initiatives, particularly from industries which are publicly perceived to produce toxic chemicals and from organisations which promote environmental sustainability.

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Public Understanding of Chemistry

Public Understanding of Chemistry: Chemistry and its social-political-economic context continue to change. Chemistry and chemistry-based technology that impact our lives make for the complexity and controversy of life and set the stage for thinking about public understanding of chemistry. The Public Understanding of Chemistry section will try to address chemistry in real life context with original contributions (articles/position papers/policy briefs) and/or published articles and columns in reputable sources (used with permission).
Founding Section Editor: David Devraj Kumar, **Section Co-Editor**: David M. Manuta

NOTHING HAS CHANGED IN ENVIRONMENTAL FORENSICS

James S. Smith
Trillium, Inc.

Abstract

Concerns over the misuse of the peer-review process to publish in order to establish expertise in environmental forensics is raised in this paper. It is time that chemists serve as the gatekeepers for environmental forensics dealing with chemistry by peer review.

Key Words

Chemistry, Environmental Forensics, Expert, Peer Review, Journal

Introduction

A dozen years have passed since I wrote a guest editorial, "Where Have All the Chemists Gone?" for "The Chemist." My beef then was with the chemistry profession, the expert witnesses encountered in environmental litigation, and the large disconnect that exists between the science of chemistry and the subject of environmental forensics. Environmental forensics is focused on three questions:

- What hazardous materials were released?
- Who released them?
- When were they released?

The last question is usually referred to as "age-dating" the release. Age-dating is very valuable information, as it often determines who is going to pay for the remediation of the release or releases. It is also a very tough answer to obtain, if, in fact, it can be obtained, and is usually arrived at through the combination of chemistry, geology, and history. The problem arises when the "expert witness" becomes an advocate for the client instead of being a professional advocate for the scientific method.

Concerns

Where are the chemists in the field of environmental forensics? Industrial chemists are not available as experts due to their affiliation with industry. Academic chemists are not inclined to testify in court because of the time constraints, stress, and negativity associated with court room opinions. This leaves the chemistry in

environmental forensics to engineers, geologists, environmental scientists, and pretty much anyone who does site environmental investigations and receives laboratory data. Many site investigations are directed by State criteria, with forensic evaluations placed in the caboose, if they are included at all.

This leaves us with a group of self-proclaimed "experts" with a wide variety of backgrounds and training, developing conceptual models of environmental chemistry that advocate for their client's innocence. To further this position, these "experts" publish their conceptual models in a peer-reviewed journal, prior to or during the litigation process. This accomplishes a deterrent from Daubert[1,2,3] or Frye[4] Hearings for their opinions.

"My opinion is correct because it has received peer-review and it has been published." Here is the crux of this story. The Daubert case in the U.S. Supreme Court made the trial judge the "gatekeeper" for scientific expert testimony in an attempt to eliminate junk science from the courtroom. One of the criteria to be used by the trial judge to ascertain the reliability and credibility of the opinions given by the expert is whether or not the scientific methodology used as the basis for the opinions has been peer reviewed.[5]

Properly used, peer review places the onus directly in the lap of scientists to keep the forensics honest to the principles of the scientific method. In other words, chemists act as the gatekeepers for environmental forensics dealing with chemistry by peer review. This is not occurring. Instead, environmental forensics articles are being given a pass without tough hard-nosed scrutiny for the data, facts and basis for the conclusions presented.

Post Script

After writing this article, I went back to the 2001 guest editorial, which has given me a title for this article. After a dozen years, I still must ask the question, where have all the chemists gone? Who let the dogs out? The gate is open and there is no one tending the gate.

IMAGE ACKNOLEDGMENT: The first image is a NIST research biologist Jennifer M. Keller taking a blood sample from a loggerhead turtle. This work is in the public domain in the United States. The second image is from Chemist Kevin Hicks, which is examining a sample of corn fiber oil for color and quality. This image was taken by Keith Weller and is in the public domain as part of the United States Department of Agriculture – USDA.
(http://patapsco.nist.gov/imagegallery/details.cfm?imageid=494, http://www.ars.usda.gov/is/graphics/photos/index.htm)

[1] *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993).
[2] *General Electric Co., v. Joiner,* 522 U.S. 136 (1997).
[3] *Kuhmo Tire Company, Ltd., v. Carmichael*, 526 U.S. 137 (1999).
[4] *Frye v. United States*, 293 F. 1013 (D.C. Cir 1923).
[5] *Ibid.*

E-CIGARETTES: BOON OR BANE?

Sue Rao
Freelance Writer

Abstract

This article aims to raise public awareness of the scientific implications of electronic cigarettes, also known as e-cigarettes or e-cigs. Although e-cigs may initially appear to be a harmless substitute for the more harmful conventional cigarette, most of the chemicals that are in e-cigs may not be harmless either. In addition, nicotine use of any sort has negative societal implications as well. Although e-cigs may sometimes be a viable stepping-stone to stop using nicotine altogether, people need to be well aware of the pros and cons of e-cigs before getting into what might become a lifelong addiction.

Key Words

Electronic Cigarette, E-Cig, Nicotine, Smoking, PV, Personal Vaporizer, ENDS.

Introduction

The electronic cigarette (or e-cigarette or e-cig) entered the U.S. market less than a decade ago after first appearing in overseas markets [1]. The e-cig is also known as a Personal Vaporizer (PV) or as an Electronic Nicotine Delivery System (ENDS) [2]. The product is spreading in availability and in variety across the United States. As the product gains market share and public attention, the e-cig is being promoted as a safe product for those who seek the pleasure of smoking without the health hazards of smoking conventional cigarettes. Studies to prove this theory have so far shown no consensus; on the contrary, they have given rise to substantial debate. Scientific and psychosocial factors both play significant parts in the debate. It remains for the individual consumer to become well-advised in order to make personal choices in their own best interest. A brief overview of conventional cigarettes might shed some light on e-cigarettes.

The Science of Conventional Cigarettes

The conventional cigarette is a small cylinder of finely cut tobacco leaves rolled in thin paper [3]. The cylinder is ignited at one end and allowed to smolder while the smoke is inhaled from the other end into the smoker's mouth. This smoke contains nicotine which triggers the brain to release dopamine, a chemical linked to feelings of pleasure. The smoker feels a temporary high [4].

However, chemicals in cigarette smoke adversely affect the entire body, causing or worsening many diseases [5, 6]. As soon as the smoke is inhaled, poisonous gases like formaldehyde start to irritate the eyes, nose and throat. Tissues of airways and lungs are damaged. Chemicals like nitrogen oxide can constrict airways, making breathing more difficult. Hydrogen cyanide, carbon monoxide and ammonia weaken the natural mechanisms that clear the lungs and airways of other dangerous chemicals, bacteria and viruses. Radioactive polonium-210 is deposited at the points where the airways split to connect to the lungs. From the lungs, cancer-causing chemicals and other poisons in tobacco smoke are absorbed into the bloodstream and then carried to the rest of the body. Many tobacco poisons such as arsenic and hydrogen cyanide can directly damage the cells that line the heart and its blood vessels. Nicotine and carbon monoxide cause blood vessels to constrict. Smoke also increases blood cholesterol, thereby increasing the chances of developing blood clots. Gases such as carbon monoxide and nitrogen oxide reduce the blood's ability to transport oxygen. The brain and other organs therefore receive less oxygen and consequently have less energy than they otherwise would. Cigarette smoke affects not only the smoker but also those nearby who inhale the smoke second-hand.

Developmental problems and a predisposition to addiction are especially experienced by babies whose mothers smoked while pregnant with them [7,8].

Ironically, however, the initial release of dopamine creates a false psychological sensation of feeling good. Even though smoking raises the heart rate, the experience may lend a false sense of relaxation if the person smokes while taking a break or while socializing with friends [4]. Social and marketing pressures directly or indirectly affect consumer groups (including youth) who anxiously seek social acceptance and easy ways to cope with the stresses of life [4, 6]. Such pressures combined with attitudes such as curiosity, naïveté and indiscretion make it very easy to try smoking even after being educated about its dangers. Once people try though, they get chemically and psychologically addicted, just as with heroin or with cocaine [4]. Although not every novice smoker finds nicotine pleasant from the first puff, peer pressure usually leads him or her to keep trying until he or she actually is addicted. Not being able to smoke causes miserable withdrawal symptoms. The next cigarette, although compounding the problems, can therefore be misperceived as a solution to this temporary discomfort. A vicious cycle is established [4] which may take decades and tremendous struggle to overcome.

The Science of Electronic Cigarettes

In light of the known dangers and restrictions of conventional cigarettes, the e-cigarette is being marketed as a substitute which releases harmless steam instead of smoke. This is why the e-cigarette is also known as a Personal Vaporizer (PV) or as an Electronic Nicotine Delivery System (ENDS). Instead of using smoldering tobacco in a paper cylinder, the e-cigarette utilizes a heating element that vaporizes a liquid solution [2] which could be simply flavored water or a combination of various chemicals including nicotine [9]. Often looking like a regular cigarette, the e-cig is claimed to provide the social and psychological pleasures of smoking without the hazards and offensiveness of smoke.

However, the safety of the chemicals vaporized in electronic cigarettes has not yet been thoroughly tested in any part of the world. According to a preliminary study performed by the FDA, manufacturers are far from having scientifically proven the safety of e-cigarettes for consumption [10]. They may present an entirely different range of dangers even if chemicals specific to tobacco smoke are absent in some e-cigarettes [9]. When adding nicotine to the mix of chemicals in e-cigarettes the risk they pose to health remains an unresolved puzzle.

Societal implications of Electronic Cigarettes

Are e-cigarettes a safe stepping-stone in the processing of quitting smoking altogether? This also is a topic of much debate. On the one hand, in an isolated study e-cigarettes were found to be at par with nicotine patches for reducing cigarette smoking [11]. On the other hand, according to the 2011-2012 National Youth Tobacco Survey, [7] among children as young as middle-school age in the United States, e-cigarette smoking was on the rise. A significant ($p<0.05$) increase in the use of e-cigarettes was noticed in the following student groups: 6-12 grades, from 3.3% to 6.8%; Middle (6-9) grades, from 1.4% to 2.7%; High school (10-12) grades, from 4.7% to 10.0%. An estimated 1.7 million students used e-cigarettes, although 160,000 of these students had "never used conventional cigarettes." This study suggests that although e-cigarettes have the potential to assist with smoking cessation, they are a growing addiction among children who have never even smoked conventional cigarettes.

Though laws and regulations for the manufacture, quality and sale of e-cigarettes are being put in place they vary widely by country and by state, and are themselves still much in debate [6, 10]. In addition, smoking and tobacco use have long been known to cause or worsen life-threatening diseases. Healthcare needs and

expenses of tobacco users skyrocket exponentially as compared to those of non-users. Efforts to educate society and to reduce the use of tobacco have put significant restraint on the availability of cigarettes (especially in the U.S.) and on the acceptability of their use in public spaces.

Summary

In summary, e-cigarettes may be both a boon and a bane, depending on the type of e-cigarette and on the context in which it is used. Some people may benefit from the use of e-cigarettes; others may not need them. Others still may be harmed. Successful cessation of nicotine use will rehabilitate the consumer's body from addiction and also the psyche from yielding to social and media pressures. All in all, a shrewd populace should recognize that the solution to one of society's largest health hazards is multifaceted and cannot be cured simply by the use or disuse of specific products.

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IMAGE ACKNOLEDGMENT: The image is from the U.S. Food and Drug Administration. The image is in the public domain and may be republished, reprinted and otherwise used freely by anyone.

MAKING CHEMISTRY FUN AT THE MUSEUM OF DISCOVERY AND SCIENCE

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Abstract

A brief outline of chemistry activities at the Museum of Discovery and Science (MODS) in Fort Lauderdale is presented. The MODS is a state of the art facility for informal science education serving Broward County, Florida school children and the general adult population for decades. Over the years chemistry activities along with activities in other branches of science have been successful in promoting public understanding of chemical sciences.

Key Words

Chemistry, Museum, Discovery, Science, Field Trip.

Introduction

The Museum of Discovery and Science (www.mods.org) in downtown Fort Lauderdale has created an exceptional space for science learning and exploration that is exciting for all ages. The Museum's mission is "to provide experiential pathways to lifelong learning in science for children and adults through exhibits, programs and films" and chemistry is definitely part of the agenda.

Visitors and students alike can enjoy science shows and presentations in the Keller Science Theater where enthusiastic staff has the ability to turn any science topic into an unforgettable experience of discovery and exploration.

Chemistry at the Museum

The science of chemistry is depicted in a fun performance setting through the live shows at the Keller Science Theater in the Museum.

- **The Nitro Show** allows visitors to discover how cold things can get with liquid nitrogen and how their physical changes can create explosive results.
- **The KaBoom! Show** offers visitors the opportunity to witness the power of chemical changes with fiery explosions. See Figure 1.

The effect of temperature and pressure is shown to the audience through the simple act of collapsing an empty soda can. The live show also teaches adults and children the about the different temperature scales and how to relate them to everyday activities.

Within the walls of the Museum, families and community organizations have the opportunity to participate in Camp–Ins, which allow each group of 40 or more the chance to discover science through hands-on activities, exploration of the Museum exhibits, while spending the night!

- Chemical Concoctions allows participants to visit the laboratory and learn all about the science of chemical changes. In the end they can even conduct their own experiments using the scientific method.

- Kitchen Chemistry teaches adults and children how chemistry is involved in an everyday task, like cooking.

Field Trips

Each year approximately 90,000 school children visit the Museum as a part of a school field trip or exploration. Discovery labs and demonstrations are incorporated into each school visit as a way to further explain important concepts for specific grades.

- Soapy Solids, Liquids, and Gases is a hands-on slippery science discovery lab program that covers the states of matter and some very unique properties of water that make it one of the most interesting molecules on earth. Surface tension is demonstrated and students learn why water is such a good solvent.
- Climate in Jeopardy is a live demonstration for students in grades six through eight. Educators cover the following topics: atmosphere, land, water and earth to see how these phenomena have influenced us, and how we influence them. By further dissecting these topics, students can better understand the structure of greenhouse gases, like CO_2, and how they act. Educators also discuss the mechanisms for heat transfer, radiation, conduction, convection, and how these affect land, ocean and atmosphere. Exhibits at the Museum in its Storm Center and in its Prehistoric Florida hall serve to enhance this demonstration.

Chemistry for Birthdays!

Museum visitors further interested in the principles of chemistry can incorporate the theme into their child's upcoming birthday celebration at the Museum. The Abracadabra Chemistry themed birthday party allows for guests to discover how chemistry might look like magic, experience a thermite reaction, make water change colors and then change them back again. Parents can also opt for their child to attend the Museum's five-day themed chemistry summer camp, where campers can learn about the various principles of chemistry in a way that applies to everyday objects.

Figure 1. The Kaboom! Show at the Museum of Discovery and Science in Fort Lauderdale.

Chemistry Outreach

The opportunity to learn about the science of chemistry is not limited to the walls of the Museum's 119,000 sq. ft. facility; rather the Museum strives to bring science to the classroom through outreach programs. Children and teachers alike have the chance to learn first-hand about the science of chemistry through the dedicated staff of the Museum's STEM Program Department.

Museum educators take The Crazy Chemistry outreach program directly into the school classroom. This program includes a chemistry demonstration that teaches students about energy, matter and physical change, highlighting the following concepts:

- Structure and properties of polymers
- physical and chemical changes
- acids and bases
- pH of solutions using litmus paper
- gases , liquids, solids and plasma
- buoyancy and density

Summary

The Museum of Discovery and Science in Fort Lauderdale is actively engaged in promoting public understanding of chemistry and the sciences in general through various chemistry activities. The activities range anywhere from in-house demonstrations to birthday parties and outreach efforts in local schools. For more information on the programs listed above, please contact Joe Cytacki, VP of Programs, Life Sciences and Exhibits at the Museum of Discovery and Science at cytackij@mods.net. For more information about the Museum, visitors should call 954.467.MODS (6637) or visit the web site at www.mods.org.

IMAGE ACKNOLEDGMENT: The logo of the museum was taken from their Web site. Figure 1 was provided by the author.

Book Reviews

Goldfrank's Toxicologic Emergencies (9th Edition)

Reviewed by Margot Hall
University of Southern Mississippi, Hattiesburg, MS 39406

This latest edition of Goldfrank's textbook may very well serve as the gold standard for books on toxicology as experienced in the emergency room setting. From start to finish it is clearly authoritative, very thorough, and oriented towards the practicing physician (house-staff, fellows, and attending physicians) and advanced medical student. It could also serve as a reference book for faculty and researchers or textbook for graduate students sitting for a specialized course (600-700 level) in clinical toxicology. The 9th edition has expanded all of its chapters and added five new chapters:

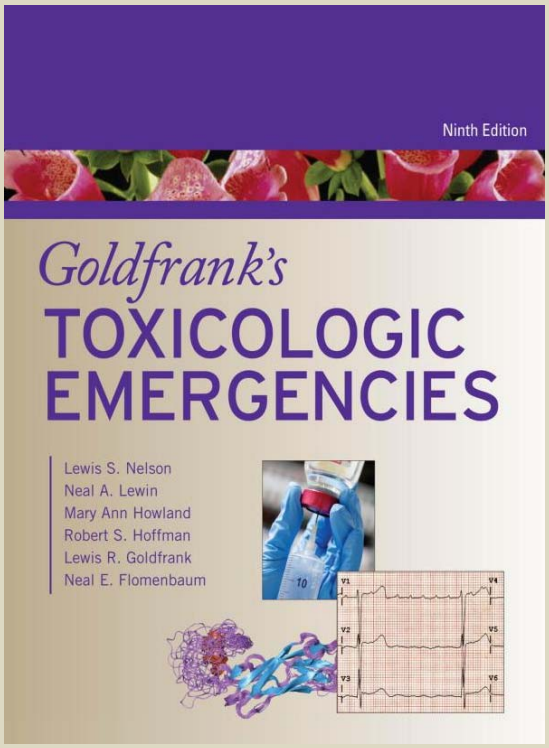
1) Chemical Principles,
2) Chemical and Biological Weapons,
3) Sports Toxicology,
4) Adverse Drug Events, and
5) Postmortem Toxicology.

It also offers case studies with extensive discussions integrated into each chapter, and a great many new case studies and annotated multiple-choice questions at the end of the book to facilitate the reader's learning.

This superb text has 6 editors, 116 contributing authors, 2170 pages, and numerous tables, figures, and photographs, including medical imaging. In addition to the table of contents and the index, there are six appendices (front and back covers) and a table of antidotes in depth. It is indubitably the most complete work of its type in the area of medical toxicology.

Each of the 120 chapters has its own list of references (~35-500 per chapter). The book is divided into five parts:

1) history of toxicology,
2) general approach to medical toxicology,
3) the biochemical and molecular basis of medical toxicology,
4) the pathophysiologic basis of medical toxicology: the organ system approach, and
5) the clinical basis of medical toxicology.



Editors:	Lewis R. Goldfrank, Neal E. Flomenbaum, Neal A. Lewin, Mary Ann Howland, Robert S. Hoffman, and Lewis S. Nelson
Publisher:	McGraw-Hill, Inc.
ISBN#:	0-07-136001-8
Year:	2010
Price:	$270.00

Part one includes two chapters detailing historical principles of toxicology and the history of plagues and disasters. Part two consists of seven chapters detailing the general principles of: 1) managing the poisoned patient, 2) identifying the nontoxic exposure, 3) preventing gastrointestinal absorption of toxic compounds, 4) enhancing elimination of toxic compounds, 5) evaluating the poisoned patient, 6) using imaging in toxicology, and 7) electrocardiography. Part three consists of seven chapters including 1) neurotransmitters, 2) pharmacokinetic and toxicokinetic principles, 3) chemical principles, 4) biochemical principles, 5) hepatic principles, 6) immunologic principles, and 7) mutagens, carcinogens, and teratogens. Part four has fourteen chapters detailing the organ system approach to toxicology including: 1) a chapter on vital signs and toxic syndromes, and 2) chapters on the principles of thermoregulation, and the neurological, respiratory, cardiovascular, gastrointestinal, renal, electrolytic and acid base, hematological, endocrine, ophthalmic, otolaryngologic, dermatologic, and genitourinary systems. Part five covers the clinical approach to medical toxicology and is subdivided into three major sections: 1) case studies in toxicologic emergencies, 2) special populations, and 3) preventive, psychosocial, nursing, epidemiologic, research, and legal perspectives. In the first section there are 74 chapters detailing specific classes of toxicants and toxins and their medical management.

Each chapter has one or more case studies with an in-depth discussion including the history and epidemiology, chemistry/pharmacology and pharmacokinetics or toxicokinetics, clinical manifestations, diagnostic testing, management, references, and summary of this class of toxicant/toxin. There is also a standalone mini-chapter on appropriate antidotes with its own set of references.

Chapters in section I are grouped according to their source as well as chemical type. Thus there are chapters on analgesics and non-prescription medications, prescription medications, psychopharmacologic medications, alcohols and drugs of abuse, food poisoning, botanicals, heavy metals, household toxins, pesticides, occupational and environmental toxins, and toxic envenomations. Section II includes 9 chapters on special patient populations including: 1) a chapter on the use of the intensive care unit for poisoned patients, and 2) chapters on pregnant and perinatal patients, pediatric patients, geriatric patients, HIV positive patients, substance users/abusers, healthcare workers, farmers, and sports/athletes. Section III has 8 chapters including: 1) chapters on psychosocial, psychiatric, and nursing principles, 2) poison information centers, 3) adverse drug events, 4) risk management and legal principles, 5) postmortem toxicology, and 6) principles of epidemiology and research design.

The book has a study guide which includes 48 pages of case studies (with answers) taken from the toxicology consultation service and 234 pages of study questions (with answers) covering the 120 chapters in the book. The book also has short appendices attached to the front and back covers. These include: 1) normal vital signs by age, 2) common equations used in the toxicology and clinical chemistry laboratories, 3) common drug and toxin-induced vital sign changes, 4) common standard laboratory values [normal reference intervals from clinical chemistry], 5) common toxicology laboratory values [normal/therapeutic level and toxic or action level], and 6) the periodic table.

Overall this book is an authoritative work that will prove exceptionally useful to practicing physicians, pharmacologists, and toxicologists working in poison control centers. It is most highly recommended for medical fellows, researchers, and graduate students who have a special interest in the area of toxicology as it relates to medical emergencies. Despite its length and extent of detail the book is very readable. It is not, however, recommended for survey courses because of the emphasis on one area of toxicology.

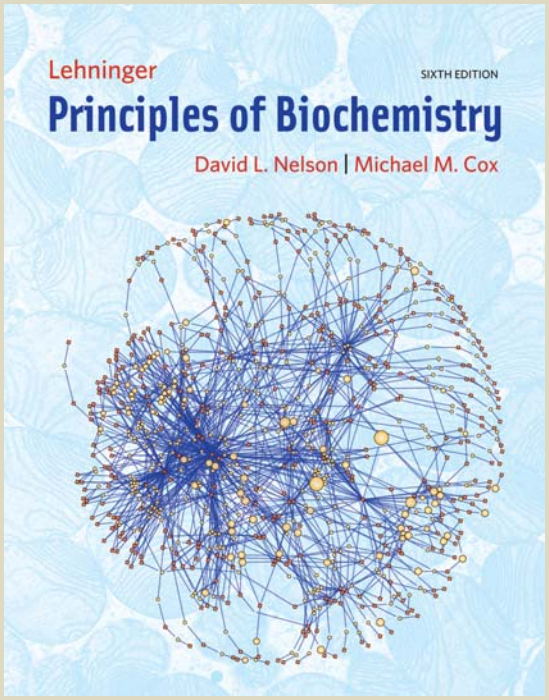
Lehninger Principles of Biochemistry 6th Edition- Instructor's Resource DVD

Reviewed by Fatimah Unnisa
Florida Atlantic University, Davie, FL 33314

The instructor's resource DVD-Rom Disk provides a comprehensive yet topic specific, computer-based support system to facilitate biochemistry instruction. It is divided into ten categories: Animated Biochemical Techniques (Adobe Flash, PowerPoint), Animated Enzyme Mechanisms (Adobe Flash, PowerPoint), Animated in PowerPoint, Art in JPEG Format, Art in PowerPoint, Clicker Questions, Lecture Presentations, Protein Database, Solutions Manual and Test Bank.

The Animated Biochemical Techniques are presented in Adobe Flash as well as PowerPoint format. This part of the software presents key cellular processes in a step-by-step or continuous play format. The step-by-step format is easy to follow and describes each process in a simple manner including all the key terms. Similarly, the software also contains key enzyme mechanisms, available in both Adobe Flash format and PowerPoint.

Another important part of the software is the lecture presentation in PowerPoint format for the entire book, starting with chapter 1 and continuing through chapter 28. The presentation includes all key topics and subtopics of the chapters along with significant captioned images of complex microscopic living matter. These provide a solid foundation on which to build your own PowerPoint lectures. Moreover, the software also includes high-resolution images in both JPEG format as well as PowerPoint.



Authors:	David L. Nelson and Michael M. Cox
Publisher:	W. H. Freeman and Company
ISBN-10#:	1-4641-0969-9
ISBN-13#:	978-1-4641-0969-0
Year:	2013
Price:	$245.95

Another convenient aspect of the software is the clicker questions for the corresponding chapters. The questions are designed to be used with "iClicker" and promote applications of biochemical terms, concepts, and laboratory methods. A helpful feature in the CD is the list of Protein Data Bank IDS for the structures in the text, arranged by figure number. Similarly, another helpful feature is the Test Bank containing both multiple-choice and short-answer problems and solutions for the purpose of testing, homework assignments and/or in-class activities.

Lastly, The CD also contains Solutions Manual (PDF) with complete worked-out solutions to all the end-of-chapter problems in the textbook. This instructor's resource is very flexible and compatible with both PC and Mac computers. The use of this software should enhance the instructor's teaching style.

The AIC Code of Ethics

Approved by the AIC Board of Directors, April 29, 1983

The profession of chemistry is increasingly important to the progress and the welfare of the community. The Chemist is frequently responsible for decisions affecting the lives and fortunes of others. To protect the public and maintain the honor of the profession, the American Institute of Chemists has established the following rules of conduct. It is the Duty of the Chemist:

1. To uphold the law; not to engage in illegal work nor cooperate with anyone so engaged;

2. To avoid associating or being identified with any enterprise of questionable character;

3. To be diligent in exposing and opposing such errors and frauds as the Chemist's special knowledge brings to light;

4. To sustain the institute and burdens of the community as a responsible citizen;

5. To work and act in a strict spirit of fairness to employers, clients, contractors, employees, and in a spirit of personal helpfulness and fraternity toward other members of the chemical profession;

6. To use only honorable means of competition for professional employment; to advertise only in a dignified and factual manner; to refrain from unfairly injuring, directly or indirectly, the professional reputation, prospects, or business of a fellow Chemist, or attempting to supplant a fellow chemist already selected for employment; to perform services for a client only at rates that fairly reflect costs of equipment, supplies, and overhead expenses as well as fair personal compensation;

7. To accept employment from more than one employer or client only when there is no conflict of interest; to accept commission or compensation in any form from more than one interested party only with the full knowledge and consent of all parties concerned;

8. To perform all professional work in a manner that merits full confidence and trust; to be conservative in estimates, reports, and testimony, especially if these are related to the promotion of a business enterprise or the protection of the public interest, and to state explicitly any known bias embodied therein; to advise client or employer of the probability of success before undertaking a project;

9. To review the professional work of other chemists, when requested, fairly and in confidence, whether they are:
    a. subordinates or employees
    b. authors of proposals for grants or contracts
    c. authors of technical papers, patents, or other publications
    d. involved in litigation;

10. To advance the profession by exchanging general information and experience with fellow Chemists and by contributing to the work of technical societies and to the technical press when such contribution does

not conflict with the interests of a client or employer; to announce inventions and scientific advances first in this way rather than through the public press; to ensure that credit for technical work is given to its actual authors;

11. To work for any client or employer under a clear agreement, preferable in writing, as to the ownership of data, plans, improvements, inventions, designs, or other intellectual property developed or discovered while so employed, understanding that in the absence of a written agreement:
    a. results based on information from the client or employer, not obtainable elsewhere, are the property of the client or employer
    b. results based on knowledge or information belonging to the Chemist, or publicly available, are the property of the Chemist, the client or employer being entitled to their use only in the case or project for which the Chemist was retained
    c. all work and results outside of the field for which the Chemist was retained or employed, and not using time or facilities belonging to a client or employer, are the property of the Chemist;

12. Special data or information provided by a client or employer, or created by the Chemist and belonging to the client or employer, must be treated as confidential, used only in general as a part of the Chemist's professional experience, and published only after release by the client or employer;

13. To report any infractions of these principles of professional conduct to the authorities responsible for enforcement of applicable laws or regulations, or to the Ethics Committee of The American Institute of Chemists, as appropriate.

The Chemist
Journal of the American Institute of Chemists

Manuscript Style Guide

The Chemist is the official online refereed journal of The American Institute of Chemists (AIC). We accept submissions from all fields of chemistry defined broadly (e.g., scientific, educational, socio-political). *The Chemist* will not consider any paper or part of a paper that has been published or is under consideration for publication anywhere else. The editorial office of *The Chemist* is located at: The American Institute of Chemists, Inc. 315 Chestnut Street Philadelphia, PA 19106-2702, Email: aicoffice@theaic.org.

Categories of Submissions

RESEARCH PAPERS

Research Papers (up to ~5000 words) that are original will only be accepted. Research Papers are peer-reviewed and include an abstract, an introduction, up to 5 figures or tables, sections with brief subheadings and a maximum of approximately 30 references.

REPORTS

Reports (up to ~3000 words) present new research results of broad interest to the chemistry community. Reports are peer- reviewed and include an abstract, an introductory paragraph, up to 3 figures or tables, and a maximum of approximately 15 references.

BRIEF REPORTS

Brief Reports (up to ~1500 words) are short papers that are peer-reviewed and present novel techniques or results of interest to the chemistry community.

REVIEW ARTICLES

Review Articles (up to ~6000 words) describe new or existing areas of interest to the chemistry community. Review Articles are peer-reviewed and include an abstract, an introduction that outlines the main point, brief subheadings for each section and up to 80 references.

LETTERS

Letters (up to ~500 words) discuss material published in The Chemist in the last 8 months or issues of general interest to the chemistry community.

BOOK REVIEWS

Book Reviews (up to ~ 500 words) will be accepted.

Manuscript Preparation

RESEARCH PAPERS, REPORTS, BRIEF REPORTS & REVIEW ARTICLES

- **The first page** should contain the title, authors and their respective institutions/affiliations and the corresponding author. The general area of chemistry the article represents should also be indicated, i.e. General Chemistry, Organic Chemistry, Physical Chemistry, Chemical Education, etc.

- **Titles** should be 55 characters or less for Research Papers, Reports, and Brief Reports. Review articles should have a title of up to 80 characters.

- **Abstracts** explain to the reader why the research was conducted and why it is important to the field. The abstract should be 100-150 words and convey the main point of the paper along with an outline of the results and conclusions.

- **Text** should start with a brief introduction highlighting the paper's significance and should be understood to readers of all chemistry disciplines. All symbols, abbreviations, and acronyms should be defined the first time they are used. All tables and figures should be cited in numerical order.

- **Units** must be used appropriately. Internationally accepted units of measurement should be used in conjunction with their numerical values. Abbreviate the units as shown: cal, kcal, µg, mg, g (or gm), %, ^{o}C, nm, µm (not m), mm, cm, cm^{3}, m, in. (or write out inch), h (or hr), min, s (or sec), ml [write out liter(s)], kg. Wherever commonly used units are used their conversion factors must be shown at their first occurrence. Greek symbols are permitted as long as they show clearly in the soft copy.

- **References and notes** should be numbered in the order in which they are cited, starting with the text and then through the table and figure legends. Each reference should have a unique number and any references to unpublished data should be given a number in the text and referred to in the references. References should follow the standards presented in the AIC Reference Style Guidelines below.

REFERENCE STYLE GUIDELINES

References should be cited as numbers within square brackets [] at the appropriate place in the text. The reference numbers should be cited in the correct order throughout the text (including those in tables and figure captions, numbered according to where the table or figure is designated to appear). The references themselves are listed in numerical order at the end of the final printed text along with any Notes. Journal abbreviations should be consistent with those presented in Chemical Abstracts Service Source Index (CASSI) (http://www.cas.org) guide available at most academic libraries.

- **Names** and initials of all authors should always be given in the reference and must not be replaced by the phrase *et al*. This does not preclude one from referring to them by the first author, et al in the text.

- **Tables** should be in numerical order as they appear in the text and they should not duplicate the text. Tables should be completely understandable without reading the text. Every table should have a title. Table titles should be placed above the respective tables.

  Table 1. Bond Lengths (Å) of 2-aminophenol

- **Figure legends** should be in numerical order as they appear in the text. Legends should be limited to 250 words.

  Figure 1. PVC Melt Flow Characterized by Analytical Structural Method

- **Letters and Book Reviews** should be clearly indicated as such when being submitted. They are not peer-reviewed and are published as submitted. Legends should be placed after/under the respective figures.

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  Booth DE, Isenhour TL. *The Chemist*, 2000, 77(6), 7-14.

- **Books -** For example:

  Turner GK in *Chemiluminescence: Applications*, ed. Knox Van Dyke, CRC Press, Boca Raton, 1985, vol 1, ch. 3, pp 43-78.

- **Patents** should be indicated in the following form:

  McCapra F, Tutt D, Topping RM, UK Patent Number 1 461 877, 1973.

- **Reports and bulletins, etc. -** For example:

  Smith AB, Jones CD, *Environmental Impact Report for the US*, final report to the National Science Foundation on Grant AAA-999999, Any University, Philadelphia, PA, 2006.

- **Material presented at meetings -** For example:

  Smith AB. Presented at the Pittsburgh Conference, Atlantic City, NJ, March 1983, paper 101.

- **Theses -** For example:

  Jones AB, Ph.D. Thesis, Columbia University, 2004.

- For material presented at a meeting, congress or before a Society, etc., but not published, the following form should be used:

  Jones AB, presented in part at the 20th American Institute of Chemists National Meeting, Philadelphia, PA, June, 2004.

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  Smith AB. *Anal. Chem*., in press

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Reference to unpublished work should not be made without the permission of those by whom the work was performed.

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The submission and review process is completely electronic. Submitted papers are assigned by the Editors, when appropriate, to at least two external reviewers anonymously. Reviewers will have approximately 10 days to submit their comments. In selected situations the review process can be expedited. Selected papers will be edited for clarity, accuracy, or to shorten, if necessary. The Editor-in-Chief will have final say over the acceptance of submissions. Most papers are published in the next issue after acceptance. Proofs will be sent to the corresponding author for review and approval. Authors will be charged for excessive alterations at the discretion of the Editor-in-Chief.

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When a paper is accepted by *The Chemist* for publication, it is understood that:

- Any reasonable request for materials to verify the conclusions or experiments will be honored.

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- The submission will remain a privileged document and will not be released to the public or press before publication.
- The authors certify that all information described in their submission is original research reported for the first time within the submission and that the data and conclusions reported are correct and ethically obtained.
- The Chemist, the referees, and the AIC bear no responsibility for accuracy or validity of the submission.

Authorship

By submitting a manuscript, the corresponding author accepts the responsibility that all authors have agreed to be listed and have seen and approved of all aspects of the manuscript including its submission to *The Chemist*.

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Announcements

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Authors are invited to submit manuscripts for ***The Chemist,*** the official online refereed journal of The American Institute of Chemists (AIC). We accept submissions from all fields of chemistry defined broadly (e.g., scientific, educational, socio-political). *The Chemist* will not consider any paper or part of a paper that has been published or is under consideration for publication anywhere else.

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American Institute of Chemists

www.TheAIC.org

From its earliest days in 1923 to the present, the American Institute of Chemists has fostered the advancement of the chemical profession in the United States.

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