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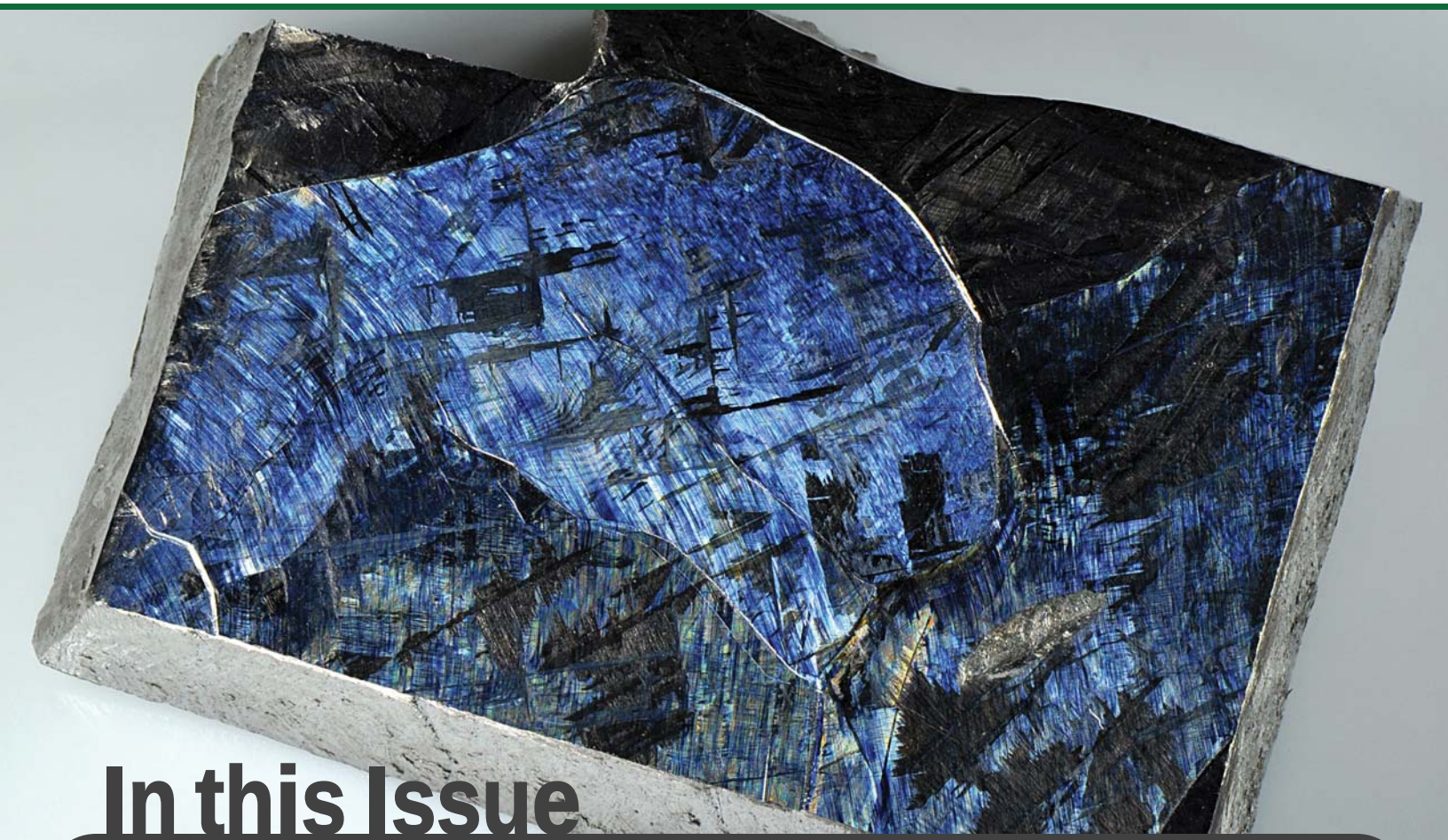

In this Issue

Note: High purity (99.999%) titanium.
This photo is part of the book "Die chemischen Elemente", SMT, 2011, ISBN 978-3-200-02434-2. This work has been released into the public domain by author Alexander C. Wimmer.
https://en.wikipedia.org/wiki/File:Hochreines_Titan_%2899.999%29_mit_sichtbarer_Kristallstruktur.jpg

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The Chemist

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The Chemist

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The Chemist (Established in 1923)

Editorial

Responsible Engagement in Chemistry

David Devraj Kumar
Florida Atlantic University

Chemistry depends upon people to define it, develop it, research it, market it, disseminate it, and regulate it. Clearly, chemistry is not limited to laboratory activities synthesizing and characterizing chemicals of various properties and applications. A range of articles on various aspects of chemistry appears in this issue: while some deal with chemical research and development, others deal with communication and reviewer bias, but they all require responsible engagement.

Two articles deal with titanium. Manayil Valappil Swapna and Karikal R. Haridas report research on a simple, inexpensive method for the low-temperature synthesis of phase-pure nanocrystalline rutile titanium dioxide. Ann M. Valentine describes how she has been exploring a possible biological role for titanium since her first year of graduate school: her contribution here is her AIC Chemical Pioneer Lecture delivered at The American Institute of Chemists meeting held in Philadelphia, Pennsylvania this year. Asraf V. Mohamed and co-authors present computational and experimental studies involving Ni(II) and Co(Ii) complexes of 1,3,4 – oxadiazole derivatives and possible application in artificial photosynthesis. Hannah Rice, and co-authors report a study comparing the diagnostic efficacy of three tumor markers (prostatic acid phosphate (PAP), testosterone (T), and prostate specific antigen (PSA) for serodiagnosis of prostate cancer.

In the Public Understanding of Chemistry section, W. Jeffrey Hurst presents communicating science, a very important topic that scientists need to be aware of. D. D. Kumar discusses a high tech weather-related application of soap bubbles. Sarah Reisert takes a historical look at The AIC Awards Program and provides a comprehensive list of winners that includes Nobel Laureates. Teri W. Odom writes "How to Remove Bias from Peer Review." This article originally appeared in *The Chronicle of Higher Education*, May 7, 2015 and is used with permission. Odem notes that the quality of the feedback provided by the reviewers determines the quality of the journal and that serving as a reviewer of manuscripts for a refereed journal is an honor. However, at times some reviewers tend to forget this fact and engage in biased and questionable behavior. An unfortunate incident in which a reviewer allegedly overstepped boundaries, prompted me to reprint, with permission, the article by Teri W. Odom. I encourage all reviewers of *The Chemist* to spend some time thinking about this article as an in-service training.

This year completes four years since I started my responsibility as the Editor-In-Chief of *The Chemist*. These four years were not without challenges, as bringing back to life a journal that was almost laid to rest was not an easy task. But it has happened, and this volume 88, issue 2 of *The Chemist* is proof that it is possible. As we move forward, my level of optimism remains high for *The Chemist* to continue to be a contributing journal to the advancement of science. Behind the scenes, Dean Valerie Bristor has been instrumental in providing the needed home base for *The Chemist* at Florida Atlantic University. Also I would like to acknowledge the feedback provided specifically by members of the review board.

Thank you

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Sonochemical Synthesis and Morphological Study of Nanocrystalline Rutile TiO_2

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Abstract: A simple and efficient methodology for the low-temperature synthesis of phase-pure nanocrystalline rutile titanium dioxide is reported in this paper. Spherical nanocrystalline rutile titania were prepared by a sonochemical method. Synthesized titania nanostructures were characterized by Thermogravimetric analysis, X-ray diffraction, Scanning Electron Microscopy, Brunauer- Emmett- Teller surface area analysis and Infrared Spectroscopy. The present study provides a simple and inexpensive way to prepare mesoporous spherical rutile TiO_2 nanoparticles.

Key Words: Sonochemical synthesis, rutile titania, thermogravimetric analysis.

INTRODUCTION

Titanium dioxide (TiO_2) is a functional material for several technological applications strongly related to its crystalline structure and morphology [1-6]. In the previous era, the main applications of TiO_2 were in the areas of pigments, catalysts and supports, fine ceramics, cosmetics, etc. After the first synthesis of nano TiO_2, its applications are tremendous and being explored in the new area of material science, including that of smart materials. For the last nearly two decades, the main applications of TiO_2 are in the field of organic electronics such as sensors, semiconductor in opto-electronic devices, including dye sensitized solar cells [7-9]. Nano TiO_2 is also being used in inorganic membranes and environmental purification systems [10-14]. The applications of nano TiO_2 are mainly due to its high chemical stability, good photo activity, wide band-gap, relatively low cost and non-toxicity.

Crystalline TiO_2 has three main polymorphs, e.g. anatase, rutile and brookite, from these rutile is thermodynamically stable phase [15]. Rutile, anatase and brookite have the same fundamental structural octahedral units with different arrangements [16]. Anatase and brookite phases are metastable and readily transformed to rutile phase when heated. Conventionally, the optical band-gap of rutile titania is 3.00eV. Therefore, theoretically it is supposed to absorb in the near UV region compared with the anatase phase. In some reports, it has been shown that rutile phase could have a higher activity over anatase when it has smaller crystallite size [17]. Rutile TiO_2 has some advantages over anatase phase, such as higher refractive index, higher dielectric constant, higher electric resistance and higher chemical stability [18]. Rutile TiO_2 has been used as the main white pigment in paints and cosmetic products and also used in capacitor, filter, power circuits and temperature compensating condensers [12]. Wang et al. reported the high photocatalytic activity of rutile TiO_2 for decomposition of rhodamine –B in water under artificial solar light irradiation [19]. Park et al. showed that the photovoltaic characteristics of rutile TiO_2 based dye sensitized solar cells are comparable to those of anatase TiO_2 based solar cells [20, 21]. Rutile TiO_2 nanoparticles can be obtained via high temperature calcination of anatase nanoparticles. However, calcination unavoidably leads to agglomeration and growth of the nanocrystalline particles [22, 23]. Hydrolysis of $TiCl_4$ in aqueous solution can form rutile nanocrystals at relatively low temperatures [24]. These methods are easily affected by the pH value and autoclaving temperature and cannot be controlled easily. Therefore the synthesis of rutile TiO_2 nanocrystals by one step method at room temperature would be significant.

Many techniques have been developed to synthesize mesoporous titania using facile template methods such as chemical implantation [25], sol- precipitation methods [26] and hydrothermal synthesis [27]. One of the most widely

used solution based nanoparticle synthesis is the sol-gel process which involves evolution of an inorganic network, known as a sol, from certain precursor materials and the consequent gelation of this inorganic network to form an ordered, three-dimensional net structure, and then the destruction of the evolved gel resulting in the formation of nanocrystalline material. The sol-gel route is very attractive because it is relatively easy to perform and allows us to tailor the morphology of particles by relative rate of hydrolysis and condensation reactions [28]. In the present work, mesoporous rutile nano titania was synthesized by an ultrasound assisted sol-gel method without any surfactant.

In recent years, ultrasonic irradiation has attracted great interest because it can produce the extreme conditions and lead to the formation of the novel structures. The sonochemical effects of ultrasound arise from acoustic cavitation, i.e., the formation, growth and implosive collapse of bubble generates localized hot spots through shockwave formation within the gas phase of the collapsing bubble. Sonochemistry is a promising preparation method that may resolve the problems arising from the conventional synthesis methods and also, this method can save energy and time, thus reducing the cost of final products. The synthesis is rapid and reproducible.

Many sonochemical methods have already been established for the preparation of titanium dioxide nanoparticles. Gedanken and colleagues reported the preparation of mesoporous titania by sonication of ethanol/ water solution containing titanium tetra isopropoxide and structure directing agent dodecylamine under ambient conditions for 6 hours [29]. Wang and co-workers have synthesized rutile titania nanocrystal by the hydrolysis of $TiCl_4$ in the presence of water and ethanol under ultrasonic irradiation at 70°C for 3 hours [30]. Amir and colleagues reported mixture of rutile and anatase nano crystal titania by sonochemical method by the hydrolysis of titanium tetra isopropoxide in ethanol using sodium hydroxide and deionised water at 50°C for 1.5 hours [31]. Hernandez-Perez and co-workers reported sonochemical synthesis of anatase tiatania nanocrystal using titanium butoxide in acetone and methanol [32]. The present method differs from the existing methods that mesoporous rutile titania nanoparticles synthesized from isopropanol without addition of surfactant and it is a room temperature reaction completed within 30 minutes.

The present work describes the synthesis of mesoporous rutile titania nanoparticles with spherical morphology by ultrasound assisted sol-gel method.
The synthesis was carried out in isopropanol using titanium tetra isopropoxide as the titanium precursor and HCl is used as the acid. The method is simple, efficient and requires low temperature.

EXPERIMENTAL

Materials

Titanium tetra isopropoxide (TIP) (Merck), isopropyl alcohol (Merck) and hydrochloric acid (Merck) have been used in the synthesis of nanocrystalline titania particles. All the reagents used were of analytical grade and no further purification was done before use.

Methods

In a preparation procedure, 2mL of titanium tetra isopropoxide was first dissolved in 20mL isopropyl alcohol by sonication for 10 minutes using high intensity ultrasonic probe (Vibronics, Ti horn, 200V) immersed directly in the reaction solution. To this solution a mixture of 1mL HCl in 9mL distilled water is added and again sonicated for 30 minutes. The clear sol formed immediately converted to a gel. The gel was then dried in the oven at 80°C overnight to evaporate the organic materials to the maximum extent. The dried crystals were calcined at 500°C for 2 hours.

Thermal decomposition nature of the sample was investigated by thermogravimetric analyzer, Perkin Elmer-TGA 4000, under nitrogen atmosphere at a heating rate of 20°C/min. X-ray diffraction analysis patterns for the phase analysis were obtained with a Rigaku Miniflex II diffractometer, using Cu-Kα radiation. The morphology of the sample was characterized by scanning electron microscope using JEOL 5600 SL microscope. N_2 adsorption- desorption measurements were done on a volumetric micrometrics tristar apparatus at liquid N_2 temperature (77.35K). The sample was treated at 300°C before measurement. On an average 33 points were taken for the sample and the average mass of the sample was 0.3g. Pore size distributions were calculated using the Barrett-Joyner-Halenda method and surface area were

calculated from the adsorption isotherm by the Brunauer-Emmett-Teller method. The average pore size was calculated from the t-plot method. Infrared spectra were measured on a Shimadzu FT-IR 8400 S spectrometer as potassium bromide disc.

RESULTS & DISCUSSION

Thermo Gravimetric Analysis (TGA)

Figure 1 shows the thermogram of synthesized titania sample before calcination. The degradation has occurred in a single step. This weight loss is due to desorption of physisorbed water and alcohol on the external surface of the crystallites. The initial weight loss is started at 50°C and is attributed to the loss of alcohol and water from the surface and the mass loss is 7.348%. There is no separate identified weight loss. However, there is a constant degradation up to 500°C. Above 500°C till 800°C, an essentially constant mass (81% sample) has been found indicating the thermal stability of the sample.

X-ray Diffraction Analysis (XRD)

Figure 2 shows the XRD patterns of calcined titania particles. The 2θ values are observed at 27°, 36°, 39°, 41°, 44°, 54°, 56°, 62°, 64° and 69°, which are in terms with the JCPDS Card Files, No. 77-0441. These peaks confirm the formation of rutile phase of titania. Based on this XRD values, the crystallite size and phase percentage of anatase and rutile can be determined [33].

The crystallite size (D) can be calculated by the Scherrer formula [34] as expressed in Eq. (1):

$$D = \frac{k\lambda}{\beta \cos\theta} \quad (1)$$

Where D is the crystallite size, λ is the wavelength of X- ray radiation, k is a constant taken as 0.89, β is the line width at half maximum height (FWHM) of the peak and θ is the diffraction angle. The crystallite size of the titania from the present sol-gel study found to be 27.7 nm.

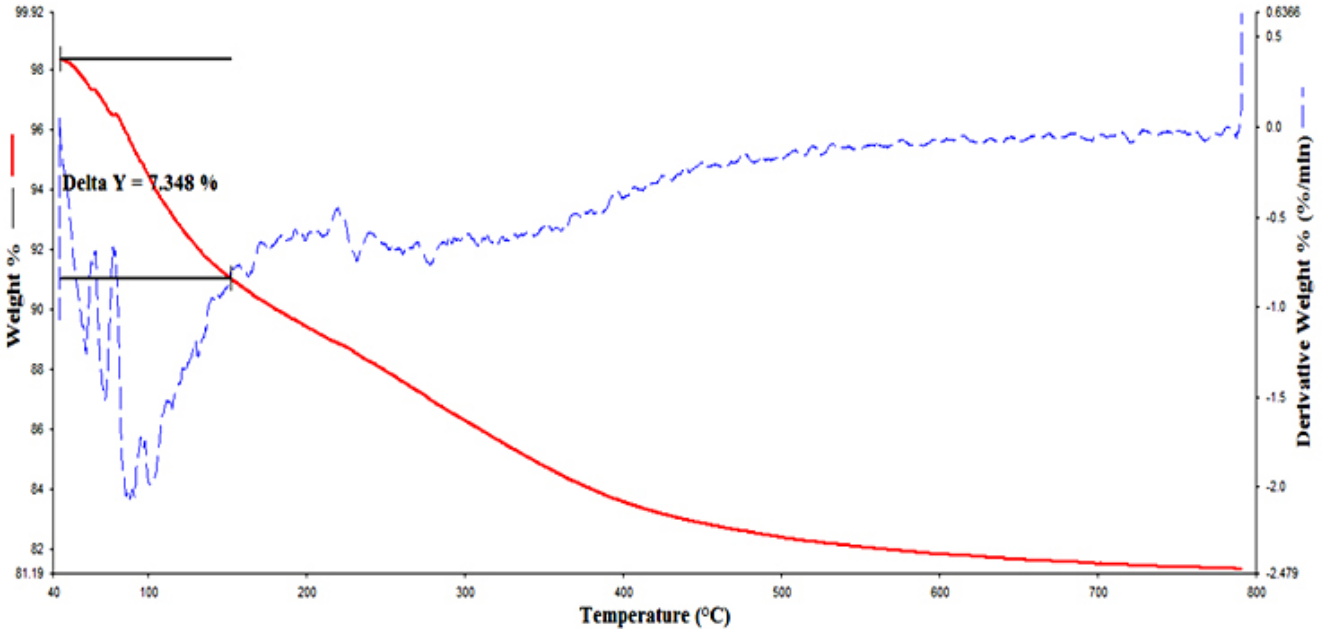

Fig 1. Thermogram of rutile TiO_2

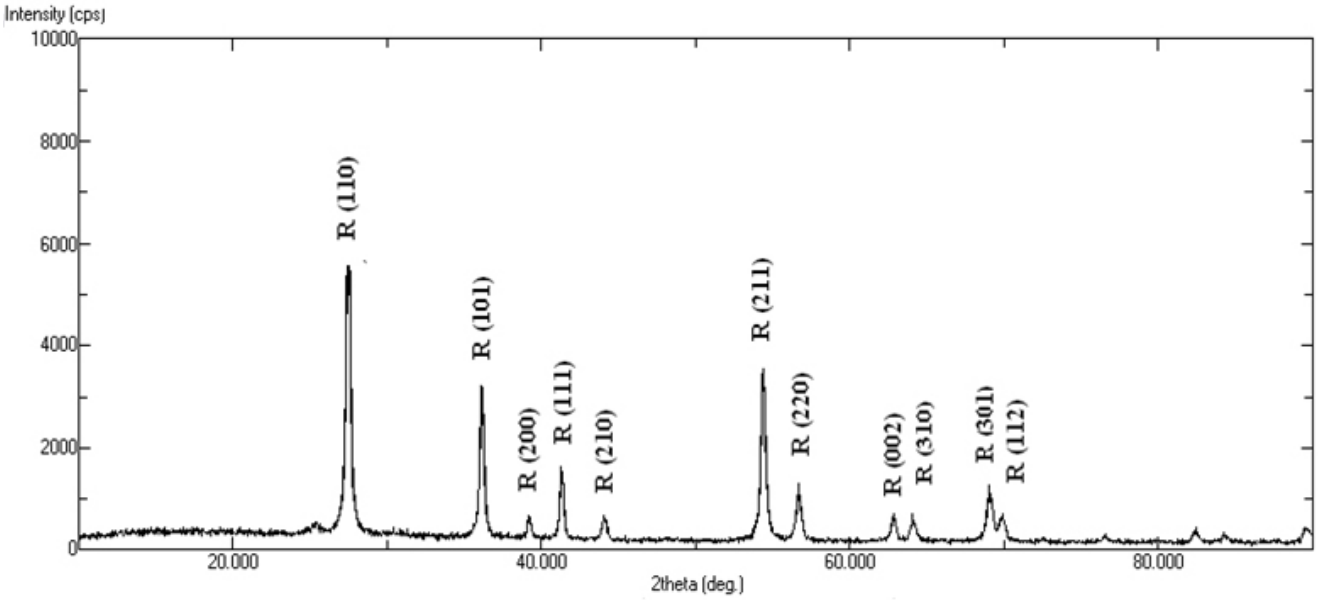

Fig 2. XRD of rutile TiO_2

Scanning Electron Microscopy (SEM)

Scanning electron microscopy (SEM) of the nanocrystalline TiO_2 was carried out to estimate the surface morphology. XRD and SEM together give the exact knowledge about the particle size and characteristics of the synthesized sample. Figure 3 shows the SEM image of the synthesized sample. As shown in the graph, the titania particle is composed of very tiny spherical nanoparticles. From the SEM image, the grain size of the nanoparticle is seen and in XRD, the crystallite size is observed. From the SEM image, titania nanoparticles with non-uniform grain size are observed.

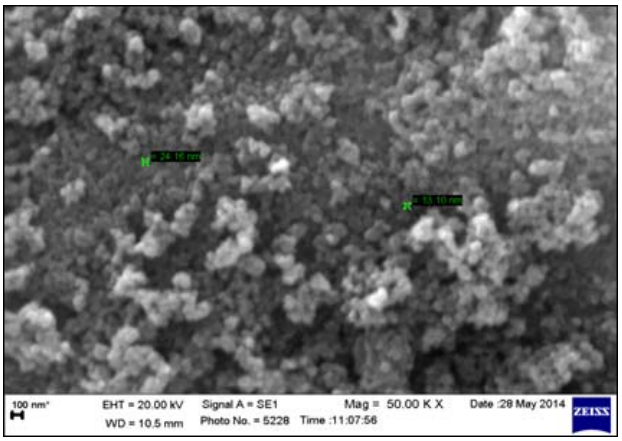

Fig 3. SEM microphotograph of rutile TiO_2

Brunauer-Emmett-Teller (BET) Analysis

BET surface area measurements were also made on the TiO_2 nanoparticle. Figure 4 shows the N_2 adsorption-desorption, which is close to type IV of the IUPAC classification with an evident hysteresis loop suggesting the sample is mesoporous. This hysteresis is an H3 type hysteresis loop in the relative pressure range (p/p_0) 0.7-1.0. Type H3 usually found on solids with a very wide distribution of pore size.

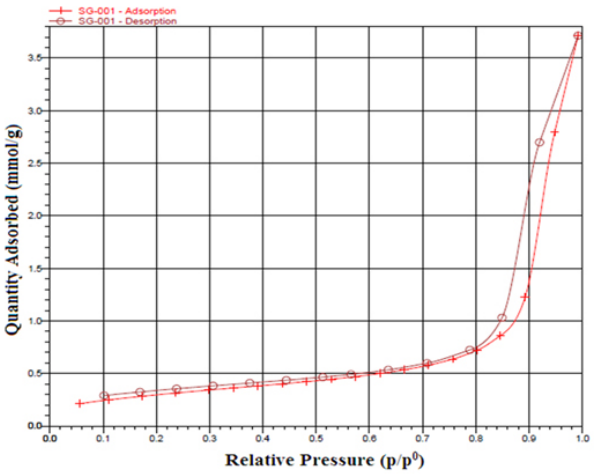

Fig 4. N_2 adsorption- desorption isotherm of rutile TiO_2

As shown in Figure 4, the capillary cohesion of TiO_2 occurred at the highest pressure, suggesting that the sample TiO_2 had the large pore size and the H3 hysteresis loop also suggested the sample had a wide pore size distribution and slit-shaped pores [35]. The specific surface area of the sample calculated by the BET method is $24.33 m^2 g^{-1}$. The pore size distribution is shown in Figure 5. The size of the most of the pores concentrate between 5 to 40nm with an average pore size of 21.1nm estimated with BJH method. The BET surface area and the pore volume were determined to be $24.33 m^2/g$ and $0.128 cm^3/g$, respectively.

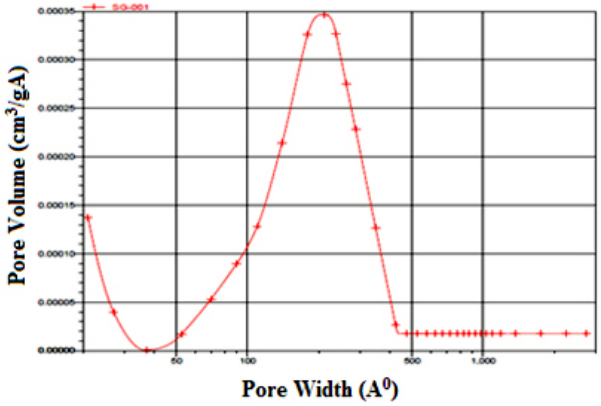

Fig 5. BJH pore size distribution of rutile TiO_2

Fourier Transform Infrared Spectroscopy (FT-IR)

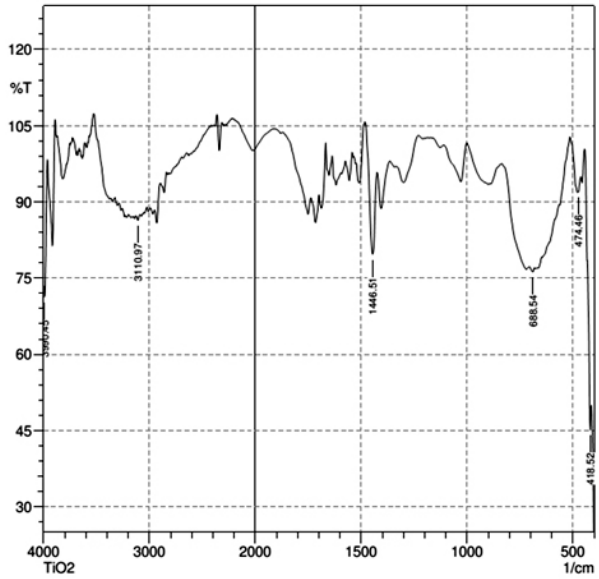

Fig 6. FT-IR spectrum of rutile TiO_2

FT-IR spectrum of synthesized titania sample after calcination is shown in Figure 6. The characteristic peaks are observed at 3110, 1446, 688, 474 and $418 cm^{-1}$. Even after the calcinations, the presence of water is observed (peak at $3110 cm^{-1}$, which corresponds to O-H stretching vibration and peak at $1446 cm^{-1}$, corresponds to O-H bend vibration of water). The Ti-O vibrations are observed at peaks $688 cm^{-1}$, $474 cm^{-1}$ and $418 cm^{-1}$ [36].

CONCLUSIONS

Pure spherical rutile titania nanoparticles were successfully synthesized using simple and cost effective sol-gel technique by ultrasonic irradiation. Ultrasonic irradiation reduced the sol-gel reaction time. The TGA analysis confirms the thermal stability of titania nanoparticles. Nearly 81% remained after 500°C. XRD shows the formation of high-purity rutile titania nanoparticles and the size is 27.7nm. Surface morphological studies obtained from SEM micrograph showed that the particles with the spherical shape. Mesoporous structure of the synthesized titania nanoparticle confirmed by BET analysis. The mesoporous titania nanomaterials could have a wide range of potential applications in catalysis and optoelectronics.

ACKNOWLEDGEMENT

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Exploring a Role for Titanium in Bioinorganic Chemistry

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Abstract: Our research in bioinorganic chemistry focuses on the uptake, trafficking, and behavior of hydrolysis-prone metal ions in biology. We present here a three-pronged approach to the investigation of titanium bioinorganic chemistry. The first focuses on biologically and environmentally relevant titanium aqueous coordination chemistry. A second area probes titanium interactions with biomolecules, especially human biomolecules. A final area centers on biological interactions with titanium in mineral form, including titanium mineralization or demineralization.

Key Words: Titanium, Bioinorganic Chemistry, Coordination Chemistry, Mineralization, Demineralization.

BACKGROUND

The story of how I came to explore a possible biological role for titanium begins in my first year of graduate school, in 1993. Our bioinorganic textbook, then recently published by my PhD advisor Stephen Lippard along with Jeremy Berg [1], featured in the first chapter a partial periodic table with "Selected elements important in bioinorganic chemistry," designated either in red (for those important in essential roles, like iron and copper) or in gray (for those important as drugs or probes, like platinum and technetium). Titanium was blank, reflecting no important biological role. At the very end of that book, though, in the last chapter the authors wrote:

Moreover, it is likely that metal ions in addition to those listed in Table 1.1 will be found to be essential elements in biology, leading candidates among the transition metals being Ti, which has been identified in a number of marine organisms….[1]

The text went on, but I was hooked. For the rest of my graduate career and during my postdoctoral work, as I worked on other problems but planned and hoped to have my own academic lab, I read and thought about a possible role for titanium in biology. Where would we find it? What would it look like? What might titanium do?

If you ask a bioinorganic chemist why certain elements are used by biology, you might get a two-part answer. First, biology uses elements that facilitate useful chemistry (reversibly carrying oxygen in blood cells, for example, or activating substrates for transformation). In this regard it would be rather surprising if biology did not use titanium; humans use titanium in various forms for many applications including as a catalyst, as a structural material, and as a pigment. The second part of the two-part answer is the more serious problem with titanium: biology uses elements that are sufficiently abundant and sufficiently bioavailable. Titanium is certainly abundant. It is the ninth most abundant element in the Earth's crust and occurs at appreciable concentrations in the oceans and in biological systems like the human body. But Ti(IV), the predominant oxidation state near neutral pH in the presence of oxygen, is a strong Lewis acid. The metal ion is prone to hydrolysis and hydrolytic precipitation in the form of titanium dioxide and related materials. The relative insolubility of Ti(IV) may thus preclude any essential biological role. The reputation of the element is certainly that it is extremely insoluble and extremely inert.

But whether or not titanium is essential for any organism, it is quite bioactive [2]. Radioactive ^{45}Ti naturally accumulates in and can be used to image solid tumors. Some titanium compounds have anticancer properties, and two of them, budotitane and titanocene dichloride, have been used in human clinical trials. Their

early promise has not yet been fulfilled, but one motivation for our work has been to understand and exploit the aqueous coordination chemistry of titanium to make compounds that preserve the anticancer activities of these compounds, but do not suffer from their dose-limiting toxicities. Various titanium compounds inhibit enzymes, affect bacterial growth, and are transported around the human body. The latter phenomenon has been studied because of the use of titanium and its alloys in biomedical implants. These implants are highly biocompatible, but it is prudent to know what happens to titanium ions that may leach or wear away from them. Some titanium compounds, particularly the titanium ascorbate formulation known as Titavit, are patented and used as growth promoters for plants and mediate weight gain in some animals. And finally, just as my first year bioinorganic textbook promised, some organisms, particularly marine organisms, contain remarkably high concentrations of titanium. The current world record holder, the ascidian *Eudistoma ritteri*, sequesters titanium in its blood at levels thirty million fold higher than the water it filters for food. We do not yet know how or why these organisms get so much titanium.

A serious inquiry into the bioactivity of titanium rests on an understanding of the aqueous coordination chemistry of Ti(IV). The ion is very Lewis acidic, and it renders any coordinated water molecules Bronsted acidic. A bound water is deprotonated below pH 0. But, contrary to conventional expectation, that hydrolysis does not necessarily equate to extreme insolubility. This ion is not as insoluble as its reputation would suggest. The neutral species invoked at pH 7, $Ti(OH)_4$, is soluble in equilibrium with amorphous hydrated TiO_2 at about 1 micromolar concentration. Coordination by complexing ligands can further increase the solubility.

The work that my lab has been doing over the past twelve years can be framed according to three key questions: What titanium chemistry can we do in water? What are important complexes, reactions, and processes related to titanium and human biology? And, because most of the titanium in the environment is in the form of metal oxide mineral materials, might organisms or biomolecules interact with mineralized titanium in the environment?

WHAT TITANIUM CHEMISTRY CAN WE DO IN WATER?

More and better aqueous- and oxygen-stable titanium complexes were required for this inquiry. We have taken inspiration from biology and stabilized Ti(IV) towards hydrolytic precipitation by using hard charged oxygen ligands like the ones nature uses to stabilize and solubilize the similarly Lewis acidic Fe(III). One of our favorite complexes is the one with citrate. Over most of its pH-dependent speciation, Ti(IV) coordinates three citrate ligands via their α hydroxy acids, making stable five-membered chelates, while two carboxylates on each ligand dangle in solution participating in protonation equilibria. Though the d^0 Ti(IV) does not offer many spectroscopic handles, methods including x-ray crystallography and electrospray mass spectrometry offer important characterization. Spectropotentiometric titrations can reveal the pH-dependent speciation. These ligands that stabilize Ti(IV) make the metal ion harder to reduce. The Ti(IV) citrate complex is very difficult to reduce electrochemically, but can be photoreduced in the ultraviolet by irradiating into the ligand to metal charge transfer band. The resulting d^1 Ti(III) is a lovely purple color and is stable if oxygen is not present in solution.

Over the years we have made Ti(IV) and, less often, Ti(III) complexes with a number of biological and bio-inspired ligands including citrate, oxalate, ascorbate, catechols and substituted catechols, and ligands that model the binding sites found in metal transport proteins like transferrin. In addition to the thermodynamic stabilities of these complexes and their properties, we have investigated the kinetics of ligand exchange under biologically or environmentally relevant conditions. In general, the multistep exchanges occur over minutes to hours.

WHAT ARE THE MEDICINAL APPLICATIONS? WHAT ABOUT INTERACTIONS OF TITANIUM WITH HUMAN BIOMOLECULES?

The anticancer activity of titanocene dichloride and butotitane was reported beginning in the late 1970s, in the wake of the tremendous success of the platinum anticancer drugs. Clinical trials began in the early 1980s, but those trials failed to progress by the late 1990s. Similar apparent mechanisms of action between titanocene dichloride and butotitane led to the proposal that these were really prodrugs, each of which served to deliver titanium, perhaps without its ligands, into a common biological pathway that mediated its anticancer activity. Hydrolysis was an undesired side reaction thought to lead to systemic dose-limiting toxicity. We and others thought that if we could figure out how to deliver titanium to whatever

biomolecule is binding it, while preventing the hydrolysis that seems to cause problems, then we could help fulfill the original promise of these compounds.

The leading contender in the early 2000s for that titanium-binding biomolecule was the Fe(III) transport protein transferrin. This protein occurs in human blood plasma. The simplest model was that the titanium compounds deliver titanium directly to transferrin, and transferrin delivers it selectively to tumor cells. In a series of papers, our lab used the well-characterized aqueous Ti(IV) coordination complexes mentioned above and showed that Ti(IV) binds to transferrin with a formal binding constant that is tighter for that for Fe(III), and that the cell surface receptor for transferrin binds titanium-carrying transferrin almost as tightly as it binds iron-carrying transferrin. These results supported the titanium-transferrin delivery model. But our work also showed that the protonation and reduction conditions that trigger Fe(III) release did not release Ti(IV) from transferrin or reduce it to Ti(III). So understanding how the titanium might get back out of transferrin and exert its action on a cancer cell was a problem. And, importantly, administering titanium-bound transferrin directly to cancer cell lines had no effect. So the original model is probably wrong, or perhaps incomplete. We are still working to understand the fate of Ti(IV) ions in the human body. We have looked at the interactions of titanium compounds with another human plasma protein, albumin, and found that the complexes bind that protein with ligands intact, and that hydrolysis and ligand loss are very much slower than in solution.

We studied a small-molecule model of transferrin called HBED (*N,N'*-di (o-hydroxybenzyl) ethylenediamine-*N,N'*-diacetic acid) which in complex with Ti(IV) has some promising activity against tumor cell lines. Moreover, this ligand provides a valuable experimental model system for titanium coordination in the metal binding site of transferrin, and gave us x-ray crystal structures related to species that we believe form in the transferrin protein as a function of pH.

As we went back and looked carefully at the literature about the human clinical trials of the titanium anticancer compounds, we noticed that there was a change in pharmaceutical formulation between the preclinical testing against cancer cell lines (in which titanocene dichloride in dimethylsulfoxide was used) and the human clinical trials (in which titanocene dichloride was formulated in a malic acid buffer in the presence of a high concentration of mannitol). We tried to reconstruct what compound or mix of compounds must have been formed in those trials by using a combination of NMR, mass spectrometry, UV/vis-detected pH-dependent speciation, and computational methods. We found that a family of similar rapidly-interconverting complexes are formed, and that these complexes interact differently with potential protein targets than the parent titanocene dichloride, in both a thermodynamic and kinetic sense. The switch in formulation in the human clinical trials probably had unforeseen consequences for compound bioactivity.

WHAT ABOUT BIOLOGICAL INTERACTIONS WITH TITANIUM IN MINERAL FORM, INCLUDING TITANIUM MINERALIZATION OR DEMINERALIZATION?

Most of the titanium in the biosphere occurs in mineral form. Again, the reputation of these materials is that they are extremely inert, but after several years of learning to prevent the precipitation of titanium, we decided to do it on purpose. The earliest known example of "biotitanification" was reported in the form of TiO_2 needles embedded in the shell of a foraminiferan called *Bathysiphon argenteus*. Because fresh material could only be obtained by dredging the Irish Sea, we convinced the British Museum in London to send us samples from the original 1913 collection. We used scanning electron microscopy data to argue that the needles were TiO_2 in its rutile form, but that they were probably selectively collected from the organism's environment and not actively biomineralized by the organism.

Meanwhile, we were reading the literature about biosilicification in the siliceous frustules of diatoms, and were pleased to see that the biomolecules controlling that biomineralization were being isolated and studied. These biomolecules included both peptides and polyamines. Knowing that titanium concentrations can be quite high in the siliceous frustules of diatoms, we set out to see whether these molecules might also mediate biotitanification from an otherwise soluble titanium source. To be clear, making titanium precipitate from solution is not challenging, but doing so in a controlled way, and being able to tune the properties of the materials that are produced, is challenging. We found that peptides and both short- and long-chain polyamines did indeed mediate or catalyze the precipitation of titanium oxide or titanium phosphate materials with sizes between 2 nm and 5 μm. We could control the particle size and properties by varying pH and temperature. And finally, we found that we could

encapsulate proteins in the titanium phosphate material induced by poly(allylamine).

In later work, we achieved the non-photochemical biotitanification of 2-5 nm amorphous titanium oxide particles inside the protein nanocage of ferritin. We complemented the microscopy and used light scattering and analytical ultracentrifugation to demonstrate that, as biomineralization proceeds inside the nanocage, the particle gets heavier while the hydrodynamic radius is unchanged.

So biomolecules can induce mineralization of titanium, but more recent work is showing, to our surprise, that very avid titanium binding ligands can do just the opposite. Such ligands can demineralize titanium. They can scavenge quite high concentrations of titanium ions from the surfaces of crystalline titanium dioxide in its anatase or rutile forms. This result was a surprise because crystalline titanium dioxide is extremely thermodynamically stable as a bulk material. However, the soluble Ti species that can be scavenged from the surface can reach into the hundreds of micromolar concentration.

CONCLUSIONS

It has now been more than twenty years since my interest was piqued by the mention in my first year graduate textbook of a possible biological role for titanium. And it has been more than twelve years since, in my own independent career, I have been able to study this problem. We have made progress, but there is much more to do.

The most important thing I hope I have demonstrated is that titanium is not just impossibly inert, as its reputation would suggest. Whether or not it is essential, the element is certainly bioactive in a variety of settings. We hope to have demonstrated convincingly that the aqueous chemistry of titanium, though challenging, can be addressed by choosing ligands that stabilize the metal ion to hydrolytic precipitation. Titanium is bioactive in humans via mechanisms that may depend on protein interactions and that are sensitive to complex formation. Understanding these interactions may ultimately help revive the early promise of the titanium anticancer molecules. Finally, organisms and biomolecules interact with titanium in its mineral forms (precipitating it from soluble precursors, binding to it, and dissolving or demineralizing it).

I'd like to close with my heartfelt thanks to all my students and collaborators over the years, and to the funding agencies that have supported our work, especially the National Science Foundation, the American Chemical Society and the American Cancer Society.

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Computational and Experimental Studies of Ni(II) and Co(II) Complexes of 1,3,4 – Oxadiazole Derivatives.

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Abstract: The Co(II) and Ni(II) complexes of 5-(pyridin-4-yl)–3*H*-1,3,4–oxadiazole-2–thione were synthesized and properties were investigated using experimental techniques and computational methods. The results indicate that the geometry of theses complexes are octahedral. IR and NMR spectroscopic characteristics and electronic spectroscopic properties of Ni(II) and Co(II) complexes of 5-(pyridin-4-yl)–3*H*-1,3, 4–oxadiazole-2–thione were investigated experimentally and computed using DFT. Computations indicate the presence of a short strong hydrogen bond in these metal complexes. A short-strong hydrogen bond is present in between the water molecule and the N-atom of the ligand, which enables the use of these kind of metal complexes in artificial photosynthesis for splitting of water. Moreover, the orbital analysis revealed that in the case of Co(II) and Ni(II) complexes, the frontier occupied molecular orbital have considerable metal orbital character.

Key Words: 1,3,4-oxadiazole, short strong hydrogen bonds, artificial photosynthesis, water splitting.

INTRODUCTION

The chemistry of 1,3,4–oxadiazoles has attracted a good number of experimental and theoretical studies in recent days [1-4]. These molecules show antimicrobial, anti-inflammatory and insecticidal properties [5-8]. There are extensive recent research reports highlighting the potential of the transition metal complexes of 1,3,4–oxadiazole dyes, photosensitive materials, liquid crystals, and inorganic light-emitting diodes [9-15]. These complexes were reported to have high electron affinities and found to have applications in OLED. Cobalt- and nickel-based transition metal complexes were explored as artificial photosynthetic systems for splitting water [16]. In natural photosynthetic systems, short-strong hydrogen bonds network with water to function as a proton exit channel [17]. These reports revealed that the Ni(II) and Co(II) derivatives of 1,3,4–oxadiazole with short strong hydrogen bonds will be effective for the development of next generation noble metal free artificial photosynthetic systems capable of splitting water. Considering the biological applications, properties suitable for developing new materials with special characteristics of 1,3,4-oxadizoles, the present work explores the electronic, spectral and orbital characteristics of Co(II) and Ni(II) complexes of 5-(pyridin-4-yl)–3*H*-1,3,4–oxadiazole-2–thione in addition to the presence of short-strong hydrogen bonds.

EXPERIMENTAL

Preparation method for the 5-(pyridin-4-yl)–3*H*-1,3,4–oxadiazole-2–thione ligand 5-(Pyridin-4-yl)-3*H*-1,3,4-oxadiazol-2-thione was prepared by cyclization of isonicotinic acid hydrazide using carbon disulphide in presence of KOH [18]. Yield: 70%, M.P: 248^{0}C, MS: m/z = 179(M+), m/z = 180(MH+). All chemicals used were of Analar grade.

Synthesis of the Ni(II) and Co(II) complexes of 5-(pyridin-4-yl)–3*H*-1,3,4–oxadiazole-2–thione analar grade chemicals were used for the synthesis of all the complexes. The Co(II) and Ni(II) complexes were prepared by adding a hot ethanolic solution of respective metal chlorides to a refluxing solution of the ligand in ethanol, maintaining the stoichiometric metal ligand ratio. The solid complexes separated out and were filtered off, washed with hot ethanol and dried (Yield 65-75 %). The complexes are insoluble in all common organic solvents except in hot DMF. The melting point of the complexes were very high (>300°C). The melting point of the ligand is 248°C. The Co(II) complex turned a brown color, while the Ni(II) complex became pale green.

Characterization Techniques

The C, H, N contents were determined micro analytically. IR spectra were recorded on a Perkin-Elmer 1600 FTIR spectrophotometer. Molar conductance of the complexes in $1x10^{-3}$ mol dm^{-3} in DMF solution were measured using Systronics microprocessor based conductivity meter at room temperature. Magnetic susceptibilities were determined with Gouy assembly at room temperature, using $Hg[Co(NCS)_4]$ as the callibrant. ^{1}HNMR (DMSO-d_6) on Perkin-Elmer R-32 spectrometer at 90 MHz.

Computational Methods

The ground state geometries of the ligand and complexes were fully optimized at DFT level using Becke's 3 parameter density functional in combination with the non-local correlation functional of Lee, Yang, and Parr (B3LYP). 6-31+G basis sets were employed for the ligand and a relativistic effective core potential of Los Alamos and Double-ζ basis sets were employed for the metals (LANL2DZ). Vibration frequency calculations were performed on the optimized geometry to verify that these molecules are minima on the potential energy surfaces. Time dependent (TDDFT) calculations were performed to obtain the vertical singlet and triplet excitation energies. Natural population analysis (NPA) and natural bond orbital (NBO) analysis [19] were performed to obtain the nature of metal-ligand bond and cation-anion interactions. All the calculations were performed using the Gaussian-09 suite of program [20].

RESULTS & DISCUSSION

Geometry Analysis of Co(II) / Ni(II) Complexes

The stoichiometries of the Co(II)/Ni(II) complexes of 5-(pyridine-4-yl)-3*H*-1,3,4-oxadiazole-2-thione were predicted by elemental analysis and molar conductance data included in Table 1. Accordingly the stoichimetries of the Co and Ni were predicted as $[CoL_2(H_2O)_2].4H_2O$ and $[NiL_2(H_2O)_2].6H_2O$. The insolubility of the complexes and their low molar conductivities in DMF indicate that these complexes are non-electrolytic and polymeric in nature [21]. Therefore, a ligand may form a complex with a metal ion with S and another with N, which indicates that there will be four ligands around Ni and Co. The observed magnetic moments of cobalt and nickel complexes are 4.87 and 3.12 BM, respectively. These results evidenced the octahedral geometry of the complexes [22-23]. The electronic spectral bands observed for the Co(II) complex at 8860 cm^{-1}, 17750 cm^{-1} and 19720 cm^{-1} are assigned to $v_1[^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)]$, $v_2[^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)]$ and $v_3[^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transitions, respectively. The ligand field parameters calculated to be 838cm^{-1} (B), 942cm^{-1}(Dq), 0.742(β) and 2.002(v2/v1). The Ni(II) complex exhibits three absorption bands at 9230cm^{-1},15050cm^{-1} and 25260cm^{-1}. These lines are assigned to $v_1[^3A_{2g} \rightarrow {}^3T_{2g}]$, $v_2[^3A_{2g} \rightarrow {}^3T_{1g}(F)]$ and $v_3[^3A_{2g} \rightarrow {}^3T_{1g}(P)]$ transitions, respectively in the octahedral geometry [24]. The ligand field parameters of B=839 cm^{-1}, Dq= 923cm^{-1}, β = 0.685 and v2/v1 value of 1.63. The results of electronic spectral analysis also gave further evidence for octahedral geometry. Considering the results of magnetic moments analysis and electronic spectral analysis of the complexes, it is confirmed that the Co(II) and Ni(II) complexes possess octahedral geometry. The ^{1}HNMR spectrum of the ligand HL recorded in DMSO-d_6 showed two doublets centered at δ 8.79 (HC-N-CH) and δ 7.77 (HC-C-CH), indicating the involvement of oxadiazole and aromatic ring in complexation.

Table 1: Mass percentage of Co, Ni, C, H, N, S along with molar conductance of Co(II) / Ni(II) complexes

	Metal (%)	C (%)	H (%)	N (%)	S (%)
Ligand	---	46.90(46.92[a])	2.76(2.79 [a])	23.43(23.46 [a])	17.85(17.87 [a])
$CoL_2(H_2O)_2].4H_2O$	11.29(11.24 [a])	32.04(32.06 [a])	4.12(4.04 [a])	16.02(16.03 [a])	12.20(12.23 [a])
$NiL_2(H_2O)_2].6H_2O$	10.53(10.50 [a])	30.07(30.02 [a])	4.42(4.5 [a])	14.83(15.0 [a])	11.41(11.47 [a])

[a] computed values

Evidence for Presence of Lattice Water

Thermogravimetric analysis (TG-DTG) of the complexes was carried out below 950°C, at a heating rate of 15°C min^{-1} under N_2 atmosphere to confirm the presence of lattice water. The results were included in Table 2. An efficient congruity has been found for the composition of the complexes on the basis of microanalysis and thermogravimetric studies. All the complexes studied thermally got decomposed at ~395°C. The presence of the water molecule (lattice/coordinated) suggested from the IR spectra is confirmed by the TG analysis. In the case of Co(II) and Ni(II) complexes, a low temperature loss of mass was recorded in the range of 50-150°C; this was followed by another between 90-300°C. These have been assigned due to the loss of lattice water and coordinated water, respectively. The other pyrolysis peaks observed have been attributed to the incomplete pyrolysis [11]. These complexes showed maximum mass loss in the temperature range of 200-500°C, corresponding to the loss of pyridine and NCO moieties. These complexes show incomplete pyrolysis in the range of study, so the final degradation step could not be determined.

Table 2. TG-DTA results evidenced the presence of lattice water in Co(II) and Ni(II) complexes

	Fragment	Pyrolysis range (^{0}C)	Pyrolysis peak ^{0}C(DTA)	Wt. Loss
$CoL_2(H_2O)_2].4H_2O$	$4H_2O$	50-90	80	14.0(13.8[a])
	$2\ H_2O$	90-130	110	7.4(6.9[a])
	2NCO	130-315	312	16.03(16.0[a])
	$2Py+Co\ (CNS)_2$	>315	350	62.7(63.0[a])
$NiL_2(H_2O)2].6H_2O$	$6H_2O$	75-150	116	19.9(19.3[a])
	$2H_2O$	150-200	190	7.5(6.4[a])
	2py	220-380	217	27.5(27.9[a])
	$2NCO+Ni(NCS)_2$	380	440	45.9(46.3[a])

Optimization of Stable Geometries of Co(II) / Ni(II) Complexes

Literature reports revealed that the 5-substituted-1,3,5-oxadiazole-2-thione may exist in two tautomeric forms [24]; the shifting of C=S stretching bands to 1200 cm^{-1} in our experimental IR spectrum also supports this observation. DFT calculations were performed with B3LYP/aug-cc-PVDZ level of theory in order to select the stable tautomer of the 5-substituted-1,3,5-oxadiazole-2-thione. The optimized structures of the two tautomeric forms along with the isolated transition states were included in Figure 1. The results of the DFT calculations revealed that the thione form shown in Figure 1(I) is more stable 10.3kcal/mol compared to the thiol form shown in Figure 1(II).The transition state isolated using QST2 possess an energy barrier of 34.6kcal/mol. Based on these results, the thione form of 5-substituted-1,3,5-oxadaiazole-2-thione is selected as the ligand for further study. The 5-substituted-1,3,5-oxadiazole-2-thione contains many potential coordination sites. The MESP is mapped on total electron density of the ligand by using ESP computations in order to optimize the active site of coordination on 5-substituted-1,3,5-oxadiazole-2-thione. When MESP is mapped on total electron density (Figure 2) of the ligand, the nitrogen of the six membered ring (indicated as N11 in

Figure 2) and sulphur (indicated as S16 in Figure 3) are more active compared to nitrogen atoms of the oxadiazole ring. The absence of N-H and S-H vibration bands near 3500 cm^{-1} to 2500cm^{-1} in the experimental IR spectral pattern confirmed this observation. Accordingly, the nitrogen (N11) and sulphur (S16) of the six membered ring are selected as the active sites for coordination. The stoichiometric characteristics, magnetic moments evaluation and electronic spectral characteristics revealed that the Co(II) and Ni(II) complexes possess octahedral geometry. Different possible geometries for the metal complexes are optimized for all the geometries at B3LYP level.

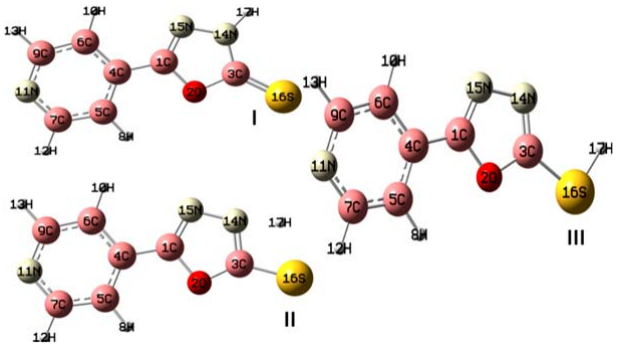


Fig 1. Optimized geometry of the tautomeric forms and intermediate transition state of the ligand 5-substituted-1,3,5-oxadiazole-2-thione

The stable geometries with no imaginary frequencies are given in Figure 3. The important optimized geometry parameters of the complexes are shown in Figure 3. The distances between the central cation and the nearest-neighboring atoms of the ligands are in agreement with previous results on similar complexes [11]. The metal atoms in Co(II) and Ni(II) complexes have a distorted octahedral coordination sphere in which the two axial M-S bonds are elongated (Figure 3). The high-spin state of cobalt and nickel (2(S+1) = 4 for Co and 3 for Ni) is evidenced from the experimental magnetic susceptibility data (4.87 BM for Co and 3.12 BM for Ni). Complexation increased the bond length of C-S bond in both Ni and Co complex by 0.06 Å. The N-N bond length of oxadizaole (oxadiazole moiety complexing with metal atom) and the metal to M-X bond distances Ni and Co complexes are 2.63and 2.70 (S), 2.16 and 2.22 (N of pyridine moiety), 2.06 and 2.07 (O of water), respectively.

An examination of frontier molecular orbitals reveals that in the case of Co(II) & Ni(II) complexes, the frontier occupied molecular orbitals have considerable metal orbital character (Figure 4); as expected from the crystal field theory which predicts that in a ML_x complex, metal d- orbitals are pushed up to become frontier occupied orbitals, whereas the ligand orbitals are stabilized because of the orbital interactions between the metal and ligand.

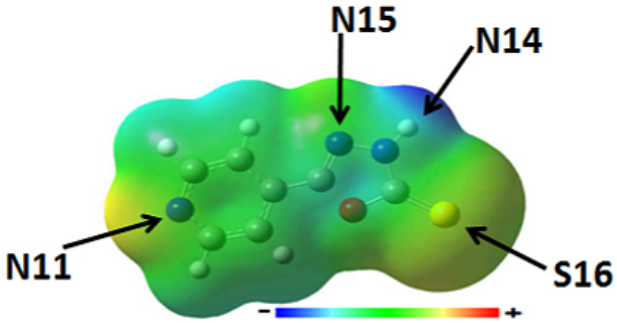


Fig 2. MESP mapped on total density of the ligand used to optimize the active site of coordination

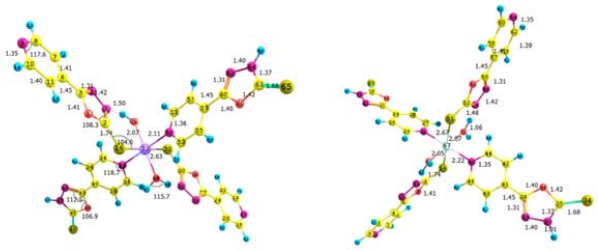


Fig 3. Optimized structures of Co & Ni Complex

IR Spectroscopic Characteristics

The IR spectroscopic characteristics were used to identify the sites of coordination and evidence for the presence of lattice water. The free ligand shows prominent bands at 1556cm^{-1}(υ(C-N) of oxadiazole ring). Computed value is 1557 cm^{-1}. The υ(C-N) in the Ni and Co complexes shows a redshift and is observed at 1542 cm^{-1} and 1519 cm^{-1} (bonded to Ni), respectively. The redshift can be attributed to complexation with metal atom [25]. The computed values are matching with experimental observations and computed to be 1579 cm^{-1} and 1528 cm^{-1}

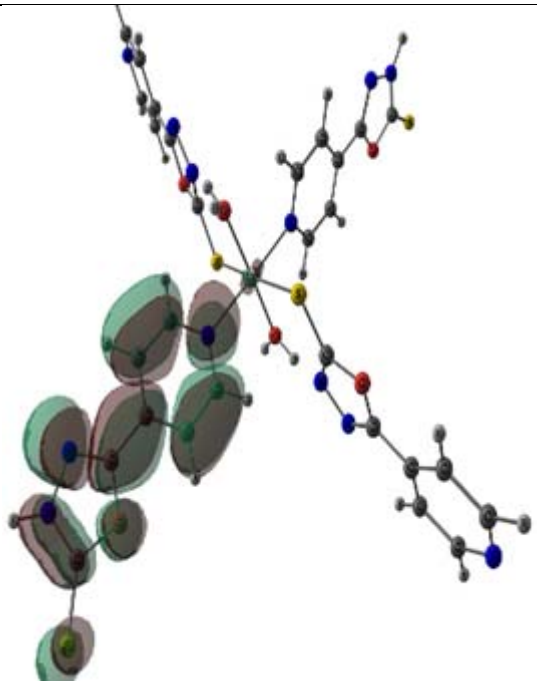
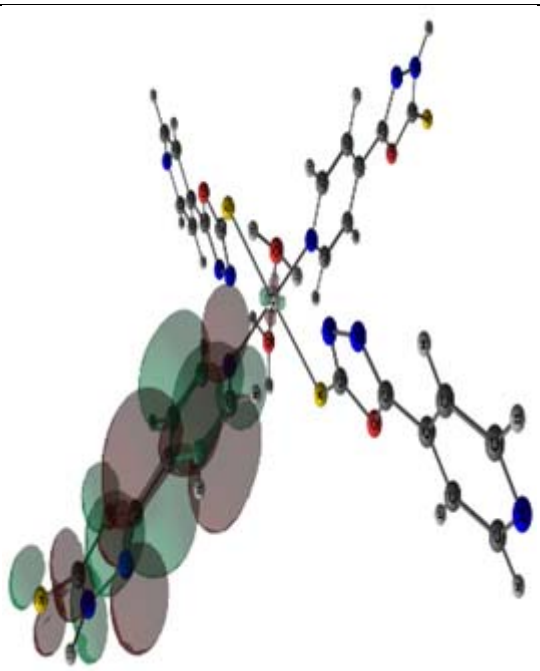
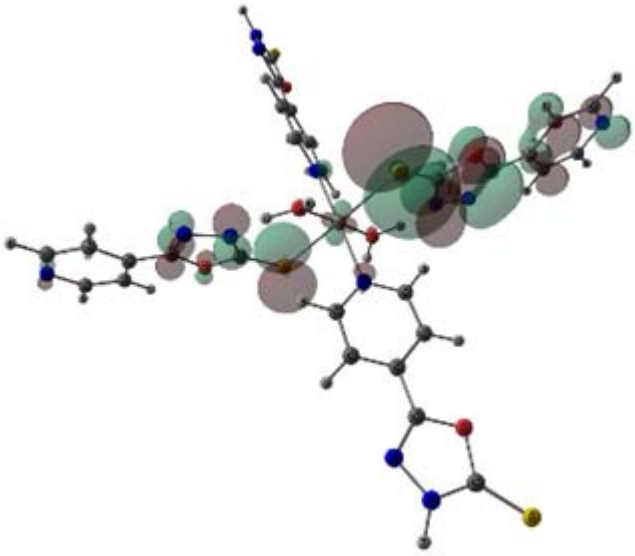
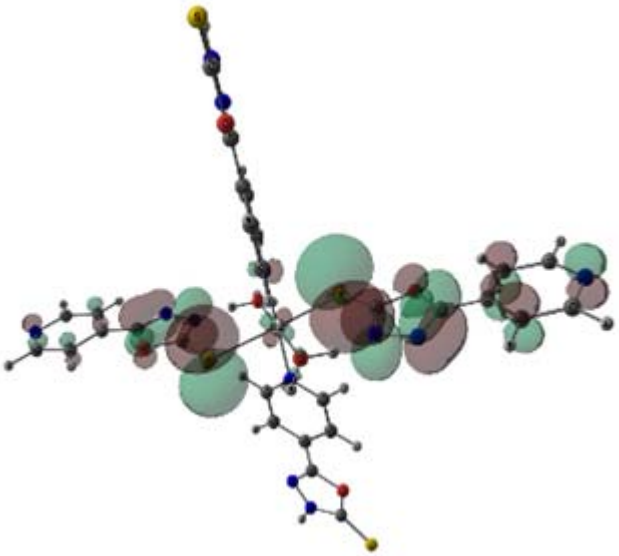
4a(i) Co Complex	4a(ii) Ni Complex
	
4a(iv) **LUMO** (E_{au} -0.1107)	4a(v) **LUMO** (E_{au} -0.1140 au)
	
HOMO (E_{au} -0.2215)	**HOMO** (E_{au} -0.2233)

Fig 4. Frontier orbitals of Co(II) complex(A) and Ni(II) complex

for the Ni complex and 1542 cm^{-1} and 1533 cm^{-1} for the Co complex. A peak was observed at 1222 cm^{-1}(1260 cm^{-1} theoretical) for the ligand, which can be assigned as δNH. In both the complexes, the frequency is redshifted by about 15 cm^{-1} and observed around 1207 cm^{-1}. Computed value is about 1260 in both complexes, and may be due to the fact that computations are done on an isolated gas phase molecule. The ligand shows a vibrational frequency at 947 cm^{-1} (theoretical 994 cm^{-1}), corresponding to the υ(N-N) vibration of the oxadiazole ring. In the metal complexes, these values also got redshifted and are about 933 cm^{-1} (computed values are around 967 cm^{-1} and 936 cm^{-1}). These data suggest that the metal interacts with the ligand through the sulphur atom. The four bands of free

ligand observed at around 1579 cm^{-1}, 1556 cm^{-1}, 1516 cm^{-1} and 1399 cm^{-1} have been assigned to C = C and C = N skeletal frequencies of the pyridine ring [11, 26]. Coordinating with metal ions, the peaks are shifted to 1587 cm^{-1} (1589 cm^{-1}), 1567 cm^{-1} (1564 cm^{-1}), 1519 cm^{-1} (1519 cm^{-1}) and 1400 cm^{-1} (1402 cm^{-1}) for the Co (Ni) complex. Computations show peaks at ~ 1579 cm^{-1} /1575 cm^{-1}, 1557 cm^{-1} /1549 cm^{-1}, 1511 cm^{-1} /1492 cm^{-1} and 1430 cm^{-1} /1437 cm^{-1} for pyrdine ring complexed and uncomplexed with the central metal atom. In the metal complex, a new band is observed around 431 in Co and 420 in Ni. Computations showed that these frequencies are corresponding to coordinated water molecule O-M vibrations, and computed values are around 413. A peak due to υPy was observed for the free ligand at 1603 cm^{-1} (theoretical 1623 cm^{-1}) [26]. The corresponding frequencies observed for Ni and Co complexes are blue-shifted to 1620 cm^{-1} and 1612 cm^{-1}, respectively. Computations indicate these frequencies are around ~1618 cm^{-1}, in agreement with the experiment values. The C-H wagging frequency was observed at 1399 cm^{-1} for free ligand and the corresponding values for Co and Ni complexes observed around the region of 1392 cm^{-1},1352 cm^{-1} and 1402 cm^{-1}, 1351 cm^{-1}, respectively. The computational values are around ~1416 cm^{-1} and ~1356 cm^{-1}, respectively. The frequency shifts indicate that the metal also complexes with ligand through the pyridine ring, as shown in the Figure 3. The broad band around 3500 cm^{-1} corresponds to OH stretching of coordinated water in both metal complexes [27]. The computed values are around 3691 cm^{-1} and 3704 cm^{-1} for the Ni and Co complexes. Although computations give frequencies to the corresponding complexed water molecule around 2210 cm^{-1} and 1639 cm^{-1} for the Ni complex and 1660 cm^{-1} and 1627 cm^{-1} for the Co complex, in experimental spectra such peaks are absent. The reason for the absence of these bands may be due to the presence of short strong hydrogen bonds, which enables shuttling of H between O of water and the ligand.

Electron Population Analysis

To describe the anion-cation interactions and charge delocalization in detail, natural population analysis (NPA) at B3LYP level was carried out. Three types of metal-ligand interactions of particular interests are σ-donation by ligand lone pairs of electron, π-donation by ligands to the metal, and π-back-bonding from metal to ligand. Computed values of NPA are given in Table 3. A striking feature observed is that the NPA charge on the nitrogen and sulphur atoms directly bonded to metal cations has a higher negative charge than that in the free ligands. For example, in the cobalt complex, the negative charge on the nitrogen and sulphur atoms bonded to metal is increased by 0.22e and 0.45e units, respectively. This kind of localization of electron density in the ligand molecule on atoms directly bonded to metal ions can be understood in terms of the possibility of stronger electrostatic interaction and electron delocalization between the ligand and metal ion. The positive charge on the cation is less in Co(II) compared to Ni(II). The extent of electron transfer from ligand anion to metal cation could be evidenced from this observation. According to the study of Reed et al. [19], a change in population of 0.001e corresponds to the change of 0.627kcal mol^{-1} in energy of stabilization. The electron transfer occurring in the nickel complex computed to be 0.69e (NPA charge). From the charge delocalizing point of view, it is concluded that large E_{CT} means strong charge delocalization from ligand atoms to cations, as well as less positive charges on cations. The NPA charges (Table 3) also supported this conclusion. The metal 3d-ligand orbital interaction, which contributes to covalent bonding in these complexes, becomes stronger in the Ni(II) than in the Co(II) complex, resulting from the increased effective nuclear charge of the metal atom in Ni(II) compared with Co(II) and the change in the 3d orbital populations. The distributions of electrons in these complexes, as determined by partial charges obtained using natural population analysis (NPA), are included in Table 3. The reduced charges on metal ions could be attributed to the nephelauxetic effect, in which the ligand charge donation partially shields the metal d electrons from the central ion nuclear charge and drives expansion of the d-electron "cloud". The identity of the metal [M (II) (M=Co, Ni)] was more clearly evidenced from the computed spin density for each complex. The excess spin on the metal was within 0.25 units of formal expectation for the respective system. The results are included in Table 4. The distribution of Mulliken spin density revealed the presence of significant spin delocalization onto the sulfur, oxygen and nitrogen atoms coordinating the metals. Most of the spin density was located within the first sphere of ligand atoms. This spin delocalization is due to the polarizability of sulfur ligands and the high spin configuration adopted by metals ions in the electronic ground state of the complexes.

Table 3. NPA derived partial charges of metal complexes

Ni-complex		Co-complex	
Atom	**Charge**	**Atom**	**Charge**
C30	+0.32	C52	0.32
N31	-0.46	N54	-0.46
S32	-0.31	S51	-0.33
C2	+0.32	C3	0.32
N3	-0.45	N14	-0.45
S16	-0.30	S16	-0.32
N33	-0.52	N31	-0.53
C 34	+0.03	C46	+0.03
C 35	+0.03	C44	+0.04
N 50	-0.52	N31	-0.53
C 51	+0.04	C29	+0.04
C 52	+0.04	C27	+0.04
H 69	+0.53	H68	+0.53
O 68	-1.07	O69	-1.08
H 67	+0.51	H70	+0.51
H 70	+0.53	H71	+0.53
O 71	-1.07	O72	-1.08

Table 4. Spin densities of selected atoms of Co(II) and Ni(II) complexes

Co(II)		Ni(II)	
S16	0.05	S16	0.09
S51	0.06	S32	0.09
N31	0.05	N33	0.06
N48	0.05	N50	0.07
O69	0.05	O68	0.04
O72	0.04	O71	0.04
Co	2.71	Ni	1.61

Evidence for Short-Strong Hydrogen Bonds in Co(II) / Ni(II) Complexes

In natural photosynthetic systems, the short-strong hydrogen bond network with water functioned as a proton exit channel [17]. The spectroscopic characteristics and orbital characteristics of the Ni(II) and Co(II) complexes revealed that strong electrostatic interaction and electron delocalization between the ligands and the metal ions were present in these complexes, a critical requirement of photo-catalytic activity. In addition to this, if these complexes possess short-strong hydrogen bonds, then this system will be effective for photo-catalytic water splitting/artificial photosynthesis. The energy profile of H-transfer between water molecule and the ligand has been computed and presented in Figure 5. Transfer of the proton from the oxygen of the water molecule to the nitrogen atom of the ligand requires only <7 kcal/mol. This result revealed the presence of short-strong hydrogen bonds [28,29]. The distance between the two heteroatoms involved in this hydrogen bond is in the range of 2.5 Å, which is much shorter compared to an ordinary hydrogen bond where the corresponding distance is ~2.8 Å. The presence of short-strong hydrogen bonds and favorable electronic properties of the Co(II) / Ni(II) complexes of 5-(pyridin-4-yl)–3*H*-1, 3, 4–oxadiazole-2–thione revealed that the two complexes would mimic the natural leaf of plants that split water in to hydrogen and oxygen.

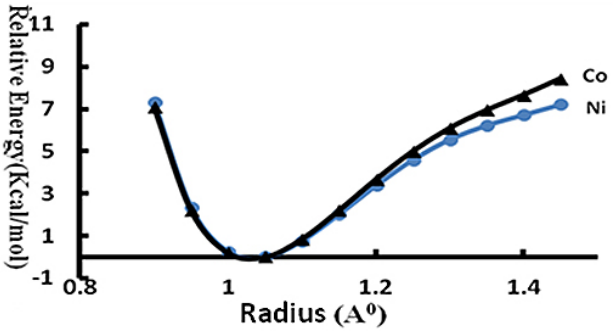


Fig 5. Calculated minimum energy path for the proton transfer from Water to Nitrogen of the Ligand in the metal complex

CONCLUSIONS

The geometry of the synthesized Co(II) / Ni(II) complexes of 5-(pyridin-4-yl)–3*H*-1,3,4–oxadiazole-2-thione complexes were predicted as octahedral by considering the stoichiometry, magnetic moments and the results of electronic spectral analysis. Moreover the two tautomeric forms of the ligand 5-substituted-1,3,5-oxadiazole-2-thione was isolated along with the transition state using DFT modeling. The results of the DFT calculations revealed that the thione form is more stable at 10.3 kcal/mol compared to the thiol form. The transition state isolated using QST2 possesses an energy barrier of 34.6 kcal/mol. ESP computations revealed that there are two coordination sites in the 5-substituted-1,3,5-oxadiazole-2-thione ligand. Considering the results of ESP

computations, electronic, IR spectroscopic characteristics and magnetic susceptibility analysis the Ni and Co complexes were modeled using DFT. Orbitals analysis revealed that in the case of Co(II) and Ni(II) complexes, the frontier occupied molecular orbitals have considerable metal orbital character. The NPA analysis revealed that strong electrostatic interaction and electron delocalization between the ligands and the metal ions were present in these complexes, a critical requirement of photo-catalytic activity. Moreover, the Ni(II) and Co(II) complex exhibited shortstrong hydrogen bonds similar to natural photosynthetic system. These results revealed that the synthesized complexes will be a potential candidate for the development of next generation artificial photosynthesis systems.

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A Comparison of Prostatic Acid Phosphatase with Testosterone and Prostate Specific Antigen for the Serodiagnosis of Prostate Cancer in Adult Males

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Abstract: The objective of this study was to compare the diagnostic efficacy of three tumor markers (prostatic acid phosphatase [PAP], testosterone [T], and prostate specific antigen [PSA]) for the serodiagnosis of prostate cancer. Immunoassay reagent test kits were obtained from Diagnostic Automation, Inc. (testosterone, prostatic acid phosphatase) and from Siemens Healthcare Diagnostics (prostate specific antigen). The prostatic acid phosphatase and testosterone assays were read using a Beckman Coulter AD 340 microplate reader. The prostate specific antigen assays were run using the Beckman Coulter Synchron LXI 725/Beckman Access instrumentation. Normal reference intervals (NRI) were developed using sera from 102 healthy adult males. Sera from 551 adult male patients (82 with cancer and 469 without cancer) were then evaluated for each of the tumor markers. The percent diagnostic sensitivity for prostate specific antigen was superior to the other two markers, whereas the percent diagnostic specificity was better for testosterone. It was concluded that prostate specific antigen was the best of these three markers.

Key Words: Prostate cancer, tumor markers, prostatic acid phosphatase (PAP), prostate specific antigen (PSA), and testosterone (T).

INTRODUCTION

Cancer is a hyperplastic cellular malignancy predicted to affect 1,658,370 people (newly diagnosed cases) in the United States in 2015 alone. The top three most frequently diagnosed forms of cancer in men have historically been lung/bronchus, prostate, and colon/rectum [1]. Oncogenesis is associated with both genetic predisposition and environmental onslaught, with a mixture of the two being required for the malignancy to progress. Birindelli et al. [2] described cancer as "the result of circumvention of the apoptotic machinery, promotion of cell division and cell proliferation, loss of cell differentiation pathways, and disruption of cell-cell communication and interaction" [2]. The resulting disease state produces malignant tissue that invades and destroys nearby tissue and can metastasize to other areas of the body [3].

Cancer is aggressive, degenerative, and affects many people worldwide. There are predicted to be 589,430 cancer deaths in 2015 in the United States alone [1]. In 1999, there were an estimated 8,100,000 cases diagnosed worldwide in that single year [4]. Cancer is classified into three categories: sarcomas, affecting bone and fibrous tissue (muscle, blood vessels); carcinomas, affecting tissues such as the epithelium, lungs, breast, and colon; and leukemias and lymphomas, affecting the cells of the bone marrow and lymph nodes [5]. Tumor markers, circulating serum factors, are used in the diagnostic screening for cancer.

Prostate cancer is a carcinoma involving the epithelial cells of the prostate, a gland in the lower abdomen of

males, just below the bladder and in front of the rectum, wrapping around the urethra. It is normally about 1.5" (3.8 cm) in diameter and produces prostatic fluid (a thick fluid that is part of semen) while simultaneously acting as a valve to allow sperm and urine to flow in the correct direction. Masses of abnormally proliferating cells swell the size of the prostate in malignant conditions and, if they breach the fibrous membrane surrounding this organ, they can quickly circulate to other tissues to produce aggressive metastasis [6]. Prostate cancer most often metastasizes to the lymph nodes, pelvic bones and spine or vertebrae, axial skeleton and proximal long bones, lungs, liver, bladder, and rectum [3].

The incidence of prostate cancer in 2015 is predicted to be 220,800 in the United States [1]. Prostate cancer is the most common cancer diagnosed in North American men [4]. It also affects thousands more in other countries worldwide. Thus, the problem of prostate cancer is both widespread and significant.

Of primary importance in the study of prostate cancer is the method of diagnosis. In addition to medical history, physical examination, and visual and tactile (such as a rectal examination) methods of tumor determination, an accurate screening test must be developed to increase early detection, efficacy of treatment, and survival rates. Alterations of genes associated with cancer provide products that can be used as molecular markers to indicate a cancer disease state [2]. Prostate specific antigen (PSA) is currently accepted as the most precise screening test for the detection of prostate cancer [7]. However, prostatic acid phosphatase was used for many years as "the most valuable enzyme marker for the diagnosis of prostate cancer," [7] because of its characteristic antigenic properties that are unlike other acid phosphatases [8]. Testosterone has also been theorized to have similar properties.

In this study, all three markers (PSA, PAP, and testosterone) were assayed in patient samples, some of which were cancerous and others which were not. The number of false positives and negatives and true positives and negatives were calculated to determine the percent specificity and sensitivity of each test. The tests were then compared by these means to determine which was the most precise for the diagnosis of prostate cancer. The objective of this study was to compare the diagnostic efficacy of PAP with that of two other markers (PSA and testosterone). It was hypothesized that PAP would prove superior to PSA and testosterone for the diagnostic screening for prostate cancer.

MATERIALS & METHODS

The kits used in this project were purchased from Diagnostic Automation, Inc. (Calabasas, CA). Tests were performed using immunoassays for prostatic acid phosphatase and testosterone. Statistical analyses were performed using SPSS version 22 statistical software. The samples were tested for prostate specific antigen at the hospitals of their origin. Permission for this study was granted by the University of Southern Mississippi Institutional Review Board under the protocol number 11080903 in accordance with Federal Drug Administration regulations, the Department of Health and Human Services, and university guidelines to ensure adherence to stipulated criteria.

Patient serum samples were obtained from two regional hospitals with only a patient number and the cancer diagnosis provided. Normal samples, obtained from a national medical center and a local regional hospital, were also utilized from persons not suspected of having cancer in order to provide a basis of comparison. All procedures detailing the confidentiality of patient medical records were followed and no information regarding the identification of a specific patient was released by the hospitals involved. Samples were collected by hospital personnel at the respective hospitals, allowed to clot, and centrifuged before being frozen and packaged in plastic tubes for transport. Before testing, all samples were sorted into test tube racks and allowed to reach room temperature.

Patient samples were classified by the hospital pathologists as either cancerous or cancer free (Table 1). This diagnosis was only provided for comparison. One hundred two normal control samples (from males in good health) were tested without bias in order to generate a normal (healthy) interval for reference.

Three test procedures were used in this experiment and consequently three sets of materials were required. Procedural instructions included with each kit were followed. The results of the assays performed in the laboratory were read with a Beckman Coulter AD 340 microplate reader. The washing of the micro-well solutions was done with a Stat Fax 2600 microplate washer. The assays performed at the provider hospitals

were done with a Beckman Coulter Synchron LXI 725/Beckman Access process.

PROSTATIC ACID PHOSPHATASE KIT

The kits, catalog #42272 and lot #12301054, used for this procedure came from Diagnostic Automation, Inc. The prostatic acid phosphatase (PAP) kit used is a quantitative solid phase enzyme linked immunosorbent assay with a detection range of 0-30 µg/mL. The test requires 50 µL of serum and performs to a specificity of 96% at a sensitivity of 1 µg/mL (as recorded by Diagnostic Automation, Inc.). The wells provided are coated with anti-PAP antibodies, and the enzyme conjugate is a mixture of anti-PAP antibodies chemically conjugated to horseradish peroxidase (HRP). The antibodies in the conjugate have different affinities toward epitopes of PAP molecules. The conjugate binds to the sample mixture in an amount proportional to the amount of PAP in the sample. Washing the solutions with the wash buffer removes any unbound conjugate. After addition of the 3,3',5,5'-tetramethylbenzidine (TMB) solution, the test mixture undergoes a light-sensitive colorimetric reaction accelerated by the HRP enzyme conjugate whose products are pigmented and allows a measurement of color intensity at 450 nm, which is proportional to the amount of bound enzyme conjugate and thus the concentration of PAP present [9].

In preparation for the assay, all reagents and samples were brought to room temperature (24±3°C) and gently mixed. The wash buffer was prepared by adding 10 mL washing buffer concentrate into 990 mL distilled water. Blanks (deionized water), calibration solutions, and controls (calibration solution of 3 ng/mL was used as the control) were run in duplicate in the first 14 wells of each kit. The remaining wells contained serum samples or extra controls. The procedures were performed according to the manufacturer's protocol (REF #4227Z) included in the purchase from Diagnostic Automation, Inc.

TESTOSTERONE KIT

The kits, catalog #RN-42074 and lot #RN-42010, used in this procedure came from Diagnostic Automation, Inc. The testosterone kit used is an enzyme immunoassay intended to quantitatively determine the concentration of testosterone in human serum. Diagnostic Automation, Inc. recorded its sensitivity to 0.05 ng/mL. This equals a concentration of 0.05 parts per billion (ppb), or 50 parts per trillion (ppt). The assay requires 10 µL of serum. Samples are dispensed into anti-rabbit IgG-coated wells and incubated with testosterone-HRP conjugate and rabbit anti-testosterone. The testosterone-HRP (fixed, known amount) competes with the testosterone in the sample to bind to the testosterone antibody (with a fixed number of binding sites). Unbound testosterone is washed away. Consequently, the detectable amount of testosterone-HRP bound to the wells decreases as the amount of testosterone in the sample increases. The 3,3',5,5'-tetramethylbenzidine (TMB) reagent added to the solution produces a colorimetric reaction which is then stopped by the addition of the stop solution (1N hydrochloric acid, HCl). The intensity of the color produced can be measured spectrophotometrically at 450 nm to determine the amount of enzyme bound to the wells, which has an inversely proportional relationship to the concentration of testosterone in the samples [10].

In preparation for the assay, all reagents and samples were brought to room temperature (24±3°C) and gently mixed. References, controls, and serum samples were run in duplicate at the beginning of each procedure. The procedures were performed according to the manufacturer's protocol (REF #2095) included in the purchase from Diagnostic Automation, Inc.

PROSTATE-SPECIFIC ANTIGEN TEST

This assay was performed in the hospital laboratories where the patient samples originated. The reagent kits came from Siemens Healthcare Diagnostics with the catalog name ADVIA Centaur Assay.

This PSA assay procedure has been labeled a "two-site sandwich immunoassay" [11] because of its use of two antibodies that "sandwich" the antigen. Constant amounts of both antibodies are used. The first antibody (a polyclonal goat anti-PSA antibody) is labeled with acridium ester, while the second (a monoclonal mouse anti-PSA antibody) has been linked to paramagnetic particles. The combination of these antibodies with the antigen (PSA) leads to a chemiluminescent reaction that can be measured in relative light units (RLUs). The amount of RLUs expressed is in direct correlation with the amount of PSA present in the patient sample. This test requires 35µL of serum and is performed automatically by the ADVIA Centaur system.

In preparation for the assay, all reagents and samples were brought to room temperature (24±3°C) and gently mixed. The procedures were performed according to the manufacturer's protocol (REF # 02676506) as purchased from ADVIA.

Table 1. Test Sample Classification

Number of Samples	Cancer Diagnosis
82	Cancerous
469	Cancer free

Total patients evaluated: 551.

RESULTS

Over the course of the project, quality control samples were incorporated into the assays to determine within- and between-run precision (Table 2). For the PAP assays, the calibrators provided were used, and additionally the provided 3 ng/mL calibrator was used as a control. For the testosterone assays, the calibrators and controls provided (control 1=0.486-1.5 ng/mL, control 2=5.2-14.0 ng/mL) were utilized. The coefficient of variation (%CV) for PSA was low (2%), but those for PAP and testosterone (41.78% and 23.29%, 10.74%, respectively) varied. Serial dilutions of patient samples were used to determine the linearity of the assays (Table 3, Figures 1-3). These results indicate good linearity, with all R^2 values near 0.98. The minimum concentration each assay is able to detect (assay sensitivity) was determined by analyzing 20 replicates of the diluent and calculating the mean ±2 standard deviation, which was established as the cut-off value (Table 4). Assay sensitivities ranged from 0.000-2.330 for testosterone.

The normal reference intervals (NRI) are given in Table 5. The NRIs were obtained by assaying sera from approximately 100 healthy adult males and calculating the mean±2SD. The intervals obtained were increased over those given in the manufacturers' inserts for the PAP assay.

In determining the normal (negative) and abnormal (positive) patient results, cut-off values from the manufacturers' inserts were used (Table 6). In this way, diagnostic sensitivities of 30.12% (PSA), 20.73% (PAP), and 0.00% (testosterone) were obtained. Sensitivities for combined markers were 30.12% (Testosterone and PSA), 43.37% (PAP and PSA), and 43.37% (testosterone, PAP, and PSA). Diagnostic sensitivity is the proportion of individuals with a disease who test positively with the test in question for that disease. The higher the sensitivity, the more accurate the test is. Similarly, diagnostic specificity is the proportion of individuals without the disease who test negatively with the test in question. Diagnostic specificities of 91.29% (PSA), 80.38% (PAP), and 96.80% (testosterone) were obtained. Combined specificities were 89.15% (testosterone and PSA), 75.11% (PAP and PSA), and 72.77% (testosterone, PAP, and PSA). Other diagnostic parameters evaluated were predictive value (+), which is the fraction of positive tests that are true positives, predictive value (-), which is the fraction of negative tests that are true negatives, and diagnostic efficiency, which is the fraction of all test results that are either true positives or true negatives.

Table 2. Assay Precision: Comparison of PSA with PAP and Testosterone using Control Sera

Within-Run

Assay	N	X (ng/mL)	SD (ng/mL)	% CV
PSA	2	1.00	0.02	2.00
PAP	20	2.13	0.89	41.78
Testosterone level 1	20	4.25	0.99	23.29
Testosterone level 2	24	19.65	2.11	10.74

Between-Run

Assay	N	X (ng/mL)	SD (ng/mL)	% CV
PSA	40	1.00	0.02	2.20
PAP	22	3.51	2.05	58.40
Testosterone level 1	15	5.11	4.69	91.96
Testosterone level 2	Not done			

Table 3. Assay Linearity: Comparison of Linearity of PSA with PAP and Testosterone

Assay	R^2
PSA	0.9996
PAP	0.9850
Testosterone	0.9830

Table 4. Assay Sensitivity: Comparison of Sensitivity of PSA with PAP and Testosterone

Assay	N	X (ng/mL)	SD (ng/mL)	Range (ng/mL)
PSA	20	0.00	0.004	0-0.008
PAP	19	0.32	0.830	0-1.980
Testosterone	20	1.21	0.560	0-2.330

Table 5. Normal Reference Intervals: Comparison of Healthy Adult Reference Intervals for Total PSA with PAP and Testosterone

Assay	N	X (ng/mL)	SD (ng/mL)	Range (ng/mL)
PSA	80	0.98	0.96	0-2.90
PAP	101	7.79	14.99	0-37.77
Testosterone	102	4.44	3.40	0-11.24

Table 6. Predictive Values (PV): Comparison of Diagnostic Parameters of PSA, PAP, and Testosterone for Prostate Cancer in 551 Patients

Tumor Marker	Sensitivity (%)	Specificity (%)	PV + (%)	PV – (%)	Efficiency (%)	Cut-off (%)
PSA	30.12	91.29	39.06	87.58	81.73	4.00
PAP	20.73	80.38	15.60	85.29	71.51	5.00
Testosterone	0.00	96.80	0.00	84.70	82.40	10.00
Combination of Testosterone & PSA	30.12	89.15	32.89	87.84	80.29	N/A
Combination of PAP & PSA	43.37	75.11	23.53	88.25	70.34	N/A
Combination of Testosterone, PAP, & PSA	43.37	72.77	21.95	87.92	68.35	N/A

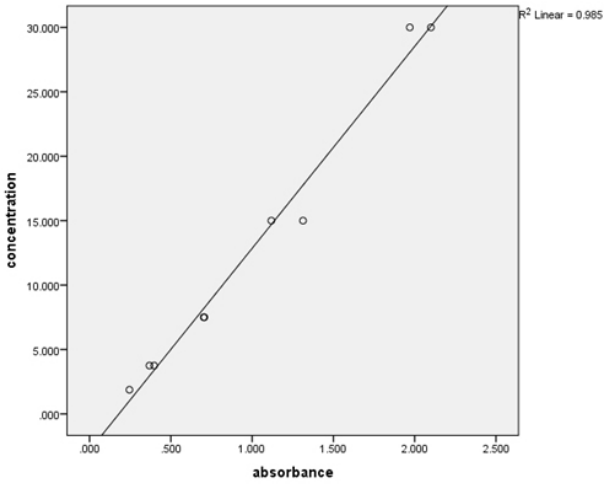

Fig 1. PAP Linearity

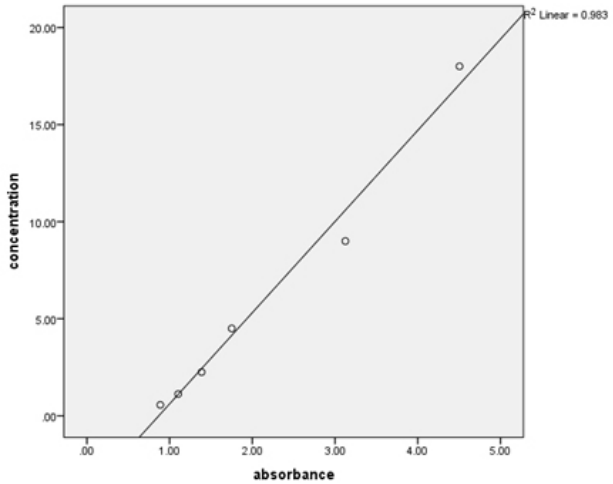

Fig 2. Testosterone Linearity

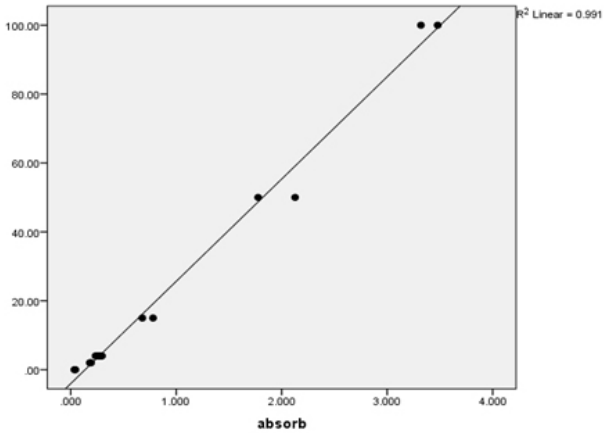

Fig 3. PSA Linearity

DISCUSSION

Analytical parameters for each of the three testing methods were adequate. As previously stated, the normal reference intervals (NRIs) calculated for PAP were significantly higher than the manufacturer's specifications. This was possibly due to a few falsely diagnosed subjects, an intrinsic defect with the testing procedure itself, or possibly a difference between the healthy sample population used to calculate the NRIs and our population due to a difference in geographical area and hence a difference in genetic mix. In an effort to test the possibility that there were one or more outliers that were causing our normal PAP results to be elevated compared with those cited by the manufacturer, we reran the data using the total sample of normal subjects (n = 101; X = 7.79; SD = 14.99), normal subjects with PAP values less than 40 ng/mL (n = 95; X = 4.80; SD = 8.68), normal subjects with PAP values less than 30 ng/mL (n = 91; X = 3.41; SD = 5.70), normal subjects with PAP values less than 20 (n = 87; X = 2.53; SD = 3.99), and normal subjects with PAP values less than 10 (n = 79; X = 1.49; SD =2.14). It was concluded that omitting 22 subjects (22%) from the normal/healthy subject pool failed to improve the SD to X ratio, but did improve the absolute NRI. From these data, it became clear that we have a non-homogeneous population of normal subjects and not simply one or two outliers. This could argue for an intrinsic defect in the testing procedure or a difference in the two populations of normal subjects. Since any adjustment of the cutoff points would inevitably affect both the diagnostic sensitivity and the diagnostic specificity, the decision was made to use the uncorrected diagnostic cutoff points provided by the manufacturers. None of the diagnostic sensitivities were optimal, but of the three examined, PSA remained the most precise by that measure. The diagnostic specificities obtained were more optimal, with testosterone representing the most specific assay (96.80%). This result was in great contrast to the 0% sensitivity of testosterone. The "cutoff points" for testosterone used were those of the manufacturer (uncorrected). PAP specificity (80.38%) was below either of the other tests (PSA-91.29%; testosterone-96%). Predictive values (+ and -) were similarly comparable. One notable result was the 0% PV+ of testosterone and its 84.70% PV- value. Consequently, it could be theorized that testosterone has more value in ruling out prostate cancer than in confirming it. PAP stayed consistently second or third in the comparison of diagnostic parameters. Testosterone had the highest diagnostic efficiency (82.40%), followed closely by PSA (81.73%).

Concerning the combined marker results, three conclusions may be drawn from the data presented. First of all, it is apparent that adding testosterone evaluation to the current measurement of PSA does not improve any of the diagnostic capabilities. Secondly, measuring both PAP and PSA improves the diagnostic sensitivity alone over that of PSA by itself. Finally, combining all three markers in diagnostic evaluation also improves only the diagnostic sensitivity over that of PSA alone.

Lee et al. [8] stated "Serum prostatic acid phosphatase has been reported as the most valuable enzyme marker for the diagnostic screening for prostate cancer." More recently however, Haese et al. [7] wrote, based on further testing, that "most experts now agree that PAP analysis has no role in the diagnosis and monitoring of prostate cancer and that PSA is clearly the superior marker." These results confirm those of our tests. While PSA does not have the ideal hallmarks of a tumor marker (high sensitivity and specificity, PV+ and -, and efficiency), it is comparably the best available within the spectrum of this study. Neither of the other markers assayed demonstrated as much consistent diagnostic screening precision as PSA. The initial statement by Lee et al. [8] that PAP is the most valuable marker was most likely made before the major discovery of the assay for PSA was widely known (Dr. Richard Albin work).

Conversely, Haythorn and Albin [12] have recently stated that the current PSA screening method is misused, leads to unnecessary treatment and anxiety and does not lead to a reduction in patient mortality. They suggest that current methods should be applied with discrimination until a replacement test can be identified. Although PAP is still used in some cases to monitor cancer progression and detect tumors that do not produce a sizable increase in PSA concentration, it has largely been replaced by PSA due to evidence reported by Haese et al. [7] and others. These latter reports are in agreement with the findings of this study.

A strong point of this study is the small number of people directly involved in testing the samples. This maintains a relatively standard amount of human error among all the testing runs and ought to render the study more reliable. Also, there was always more than one person present during testing to serve as backup to prevent pipetting error. All the testing kits for each tumor marker were obtained from the same company, standardizing the potential equipment error. Conversely, the age of some of the samples is a possible weakness due to potential sample degradation. Those samples from the national hospital were several months old, in contrast to the more recent samples from the regional hospitals. To improve the precision of this study, a larger number of samples should be tested from multiple geographic regions. The samples used should be as fresh as possible, and only thawed once, when tested.

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COMMUNICATING SCIENCE

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Uncle Tungsten [1] recounts the experiences and development of a young man who loved chemistry. The author, Oliver Sacks, decided against becoming a chemist in order to become a world-famous neurologist and author who, in addition to Uncle Tungsten [1], wrote a number of books such as The Man Who Mistook his Wife for a Hat [2] and Awakenings [2]. Depending on your level of interest in science topics, you also may have read one of the many volumes written by Carl Sagan or the book about the biotech industry titled NO by Carl Djerassi [4]. (This is obviously not a complete list, but it is used for illustrative purposes.)

The purpose of the title, *Communicating Science*, and the resulting introduction proceeded from a conversation with some colleagues who were not from the science arena. While discussing some of the developments, I felt obligated, since I am an analytical chemist, to rattle off a list of the newest instrumental techniques and developments. When their eyes started to glaze over, I knew that I was done and, no matter how glitzy or impressive the techniques, they were underwhelmed. Whether you are a student of the writings of Carl Sagan, Oliver Sacks, or Carl Djerassi is immaterial; what they and many others have excelled at is the ability to communicate not only science, but also the excitement of science to the general public. Unfortunately, many in the science community feel that these efforts tend to "dumb down" science and make it less pertinent. Fortunately, those who think so are incorrect. One must also be aware that there are a number of individuals on all sorts of communication sources, ranging from TV to the ever-expanding Internet, who dispense scientific information of varying quality. Furthermore, there are still educators who use some of the basic science courses as a method to eliminate those who they feel are unworthy.

One the most evident trends is the increasing use of acronyms in all areas of life, science becoming one of the biggest users. An obvious and important use of acronyms is providing colleagues with a shorthand way of communicating. However, things sometimes go too far, resulting in confusing acronyms which perform the exact opposite function as initially planned. To add confusion to the mix, some cannot even guess the real meaning for the various words which now populate the environment, such as names for utilities (e.g., Verizon), drugs, and new cars.

As a practicing scientist, I feel that one of my responsibilities is to not only perform excellent science, but also ensure that we work to communicate developments in science to those who are not in the field. Many times when asked, "How are you?" I respond with, "Science is wonderful." Although this is true, we must not get too

engrossed in our own efforts that we fail to communicate. It is important that we all cultivate the ability to communicate since this is critical for funding, participating in governmental programs and organizations, and developing public support for a position. For example, ACS has a program which alerts you when items of legislation pertaining to funding for various programs are under consideration. Since we all like to think of ourselves as interested in government, this alert is very timely, for we cannot know the total legislative agenda. You can use this information to provide your personal opinion to your Congressman or Senator, which may affect their vote as well as the outcome of the bill in question. The same kind of approach can be used for legislation in other states, but would require more vigilance as there is no general alerting service available. The ability to communicate to these individuals is critical since they are interested in your concise viewpoint, not a copy of your dissertation.

When talking with friends and colleagues outside the science arena, a discussion may easily turn to a topic where you could provide some assistance. For example, the term *genomics* is used in everyday conversation, but some are unaware of what it is or means. It is simply another buzzword. I can almost envision a late-night host asking, "What is genomics?" with the answer, "It was in *The Lord of the Rings*." The ability to communicate scientific concepts clearly is critical and helps us as various fields develop at a breathtaking pace.

In summary, I hope that this will give you cause to think on the topic of communicating science – its impact on our lives and what you can do to contribute.

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A LOOK INSIDE THE AIC AWARDS PROGRAM: THE GOLD MEDAL & CHEMICAL PIONEER AWARDS

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Introduction to the AIC Awards

Abstract

The awards program of the American Institute of Chemists has an illustrious history dating back to 1926. This article details the history of the AIC Gold Medal and AIC Chemical Pioneers in particular, and includes comprehensive lists of winners for both awards up to and including 2015.

Key Words

Gold Medal, Chemical Pioneers, awards.

The author has what could be considered an unusual day job: she manages an awards program. The Chemical Heritage Foundation in Philadelphia, where she works, presents eight to ten awards each year, for subjects ranging from petrochemistry to biotechnology to scientific instrumentation. Another is a public lecture; yet another is for a book. Needless to say, she gets to meet a lot of very interesting people.

Many of the awards are presented jointly with CHF's affiliates. For example, it is her responsibility each year to assist the American Institute of Chemists with their annual presentations of The AIC Gold Medal and The AIC Chemical Pioneer Awards. The awards partnership between The AIC and CHF began in 2003, and cemented our organizations' longstanding friendship through our mutual desire to honor extraordinary scientists.

The process for selecting winners for The AIC Gold Medal and Chemical Pioneer Award is straightforward. In the early fall, the chair of The AIC awards committee sends out a call for nominations. The nominations are sent to her office and consist of a letter of a nomination and two letters of support. Once she collects any and all nominations, she sends them to the chair who distributes them to the awards committee. The committee members reflect upon their choices, and each secretly sends their top three selections to her. When she has tallied them all, she sends the results to the chair and a winner is declared.

She is proud to be a small part of these awards with such long and illustrious histories, which she is pleased to share here with readers of *The Chemist*.

The AIC Gold Medal

The name William Blum might not ring a bell with many people today. Blum was a native of the author's hometown, Philadelphia. In black and white pictures, he has a long, friendly face and eyes framed by wire-rimmed glasses. According to the Electrochemical Society, of which he was president in 1926 and 1927, "His many research accomplishments involved: the atomic weight of cadmium; complex inorganic acids; electrochemistry; electrodeposition; electrotyping; electroplating; and electroforming. Dr. Blum was one of the most highly respected authority's [*sic*] on electrodeposition in his day."

It was because of this pioneering work in electrochemistry that he was the first recipient of The AIC Gold Medal, the organization's highest award. The medal is presented each year to a person who has stimulated activities of service to the science of chemistry or the profession of chemist or chemical engineer in the United States of America. In 1926 that person was Bill Blum, beginning a tradition of honoring scientific excellence that continues to this day.

The full list of impressive winners can be found in Appendix A and is definitely worth a look. It is a tour through the greatest chemists of the twentieth and twenty-first centuries, and includes a dozen Nobel laureates. To give you a small idea of the caliber of scientist that has won the Gold Medal, here is a standout medalist from each decade:

- **1930**: George Eastman, photography pioneer
- **1949**: Warren K. Lewis, the father of modern chemical engineering
- **1955**: Carl Marvel, one of the world's outstanding organic chemists
- **1969**: Henry B. Hass, discoverer of gas chromatography
- **1973**: Glenn Seaborg, co-discoverer of ten elements
- **1987**: Arnold Beckman, instrumentation pioneer
- **1998**: F. Albert Cotton, arguably the most influential inorganic chemist to ever live
- **2004**: Carl Djerassi, without whom we wouldn't have the birth control pill
- **2012**: Elizabeth Blackburn, co-discoverer of telomerase

It should also be noted that The AIC Gold Medal was the first major chemistry award presented to a woman, Mabel Brady Garvan. Garvan, along with her husband, were recognized in 1929 for their work with the American Chemical Society and the Chemical Foundation. (Further, she and her husband established their own award with John Olin which to this day recognizes the contributions of women scientists.) Two of the last four Gold Medalists have been women as well, showcasing the AIC's commitment to diversity.

Today, The Gold Medal is presented jointly with the Chemical Heritage Foundation at Heritage Day, CHF's annual celebration of the achievements and promise of the sciences and technologies that shape material culture. Hundreds of people attend.

The AIC Chemical Pioneer Award

The Gold Medal is not the only award presented by the American Institute of Chemists, though it is the oldest. Its younger brother, so to speak, is the Chemical Pioneer Award. First given in 1966, the Chemical Pioneer Award recognizes chemists and chemical engineers who have made outstanding contributions advancing the science of chemistry or impacting the chemical industry or the chemical profession. Several illustrious scientists can win the Chemical Pioneer Award in any given year; though most years honor two or three, the most ever given in a single year is seven. That record year was 1966, the first year of the Chemical Pioneer Awards.

The list of past winners of the Chemical Pioneer Award is no less illustrious than that of The AIC Gold Medal. Nine Chemical Pioneers are recipients of the Nobel Prize—six of whom were honored with the Chemical Pioneer Award years or even decades before they went on to win their Nobel Prizes. The full list is available in Appendix B, but here is a standout winner from each decade:

- **1969**: Roy Plunkett, inventor of Teflon
- **1977**: Donald Othmer, founding editor of the landmark *Kirk-Othmer Encyclopedia of Chemical Technology*
- **1980:** Stephanie Kwolek, inventor of Kevlar
- **1992**: Ralph Hirschmann, leader of the team that produced the first organic synthesis of an enzyme
- **2005:** Bassam Shakhashiri, renowned science educator and demonstrator
- **2014:** Robert Langer, the most cited engineer in history

The Chemical Pioneer Awards are presented each year at The AIC Annual Meeting. This generally takes place the day after Heritage Day (at which the Gold Medal is presented), making for quite a celebratory week.

End Note

Except Mabel Brady Garvan in 1929 noted earlier, until recent times all the award recipients have been males. Mindful of this quite unfortunate gender gap left unattended over decades, The AIC Awards Committee under the chairmanship of Dr. David Devraj Kumar has been making every effort to increase the nominations of stellar women in the chemical sciences who have made significant, noteworthy scientific contributions. As a result, the number of women receiving The AIC Gold Medal and The AIC Chemical Pioneer awards has been steadily on the rise.

The year 2016 is both the 90th anniversary of The AIC Gold Medal and the 50th anniversary of The AIC Chemical Pioneer Award. These are landmarks that few awards achieve while still retaining their relevance, so it is a cause for celebration indeed. The author looks forward to working with The AIC during the anniversary year, and indeed every year, as The Institute recognizes those scientists who have changed the world are honored.

Postscript

The author, Sarah Reisert, is the Awards Program Manager at the Chemical Heritage Foundation. The lists of previous The AIC Gold Medal winners (Appendix A) and The AIC Chemical Pioneer Award winners (Appendix B) are compiled from the following published sources. *Previous Gold Medal Award Winners,* American Institute of Chemists, Philadelphia, PA, (http://www.theaic.org/awards_goldmedal.html), and the *Previous Chemical Pioneer Award Winners*, American Institute of Chemists, Philadelphia, PA, (http://www.theaic.org/awards_chem_pioneer.html). It should be noted that some of The AIC award recipients have received the Nobel Prize before or after receiving The AIC awards.

Appendix A - Winners of The AIC Gold Medal, 1926-2015

2015 Dr. Jacqueline K. Barton
2014 Dr. Ronald C. D. Breslow
2013 Dr. John Roberts
2012 Dr. Elizabeth Blackburn (Nobel Prize, 2009 Physiology or Medicine)
2011 Dr. Dudley Herschbach (Nobel Prize, 1986 Chemistry)
2010 Dr. Robert Grubbs (Nobel Prize, 2005 Chemistry)
2009 Dr. Oliver Smithies (Nobel Prize, 2007 Medicine)
2008 Dr. Paul Berg (Nobel Prize, 1980 Chemistry)
2008 Dr. Walter Gilbert (Nobel Prize, 1980 Chemistry)
2007 Dr. George Whitesides
2006 Dr. Roald Hoffman (Nobel Prize, 1981 Chemistry)
2005 Mr. Robert L. McNeil, Jr.
2004 Dr. Carl Djerassi
2003 Dr. Ralph Hirschmann
2002 Dr. Tobin Marks
2000 Dr. Yie W. Chien
1998 Dr. F. Albert Cotton
1997 Dr. Alfred Bader
1996 Dr. Harry Drickman
1995 Dr. George Parshall
1994 Dr. Arthur Adamson
1993 Dr. Fred Basolo
1992 Dr. Roy L. Whistler
1991 Dr. Bruce N. Ames
1990 Dr. Harry B. Gray
1989 Dr. Elias J. Corey (Nobel Prize, 1990 Chemistry)
1988 Dr. George C. Pimentel
1987 Dr. Arnold O. Beckman
1986 Dr. N. Bruce Hannay
1985 Dr. Herbert C. Brown (Nobel Prize, 1979 Chemistry)
1984 Dr. John H. Sinfelt
1983 Dr. Mary L. Good
1982 Dr. Milton Harris
1981 Dr. Lewis Sarett
1980 Dr. Arthur M. Bueche
1979 Dr. Melvin Calvin (Nobel Prize, 1961 Chemistry)
1978 Dr. Norman Hackerman
1977 Dr. Max Tishler
1976 Dr. Kenneth S. Pitzer
1975 Dr. William O. Baker
1974 Dr. W. E. "Butch" Hanford
1973 Dr. Glenn T. Seaborg (Nobel Prize, 1951 Chemistry)
1972 Dr. Harold C. Urey
1971 Dr. Emmett B. Carmichael
1970 Dr. Willard F. Libby (Nobel Prize, 1960 Chemistry)
1969 Dr. Henry B. Hass
1968 Dr. Orville E. May
1967 Dr. Wayne E. Kuhn
1966 Dr. John H. Nair
1965 Brig. Gen Edwin Cox
1964 Dr. Roger Adams
1963 Dr. Ralph Connor
1962 Dr. George W. Parks
1961 Dr. Alden H. Emery
1960 Dr. Ernest H. Volwiler
1959 Dr. Crawford H. Greenewalt
1958 Dr. Lawrence Flett
1957 Dr. Roy Newton
1956 Mr. Raymond Stevens
1955 Dr. Carl S. Marvel
1954 Dr. William J. Sparks
1953 Dr. J. C. Warner
1952 Dr. Fred J. Emmerich
1951 Dr. Harry N. Holmes
1950 Dr. Walter J. Murphy
1949 Dr. Warren K. Lewis
1948 Dr. Charles A. Thomas
1947 Dr. Moses Leverock Crossley
1946 Mr. Robert Price Russell
1945 Dr. John W. Thomas
1944 Dr. Willard H. Dow
1943 Dr. Walter S. Landis
1942 Dr. William Lloyd Evans
1941 Dr. Henry G. Knight
1940 Dr. Gustav Egloff
1938 Dr. Frederick G. Cottrell
1937 Dr. James F. Norris
1936 Dr. Marston Taylor Bogert
1934 Dr. James Bryant Conant
1933 Dr. Henry C. Sherman
1932 Dr. Charles H. Herty
1931 Mr. Andrew W. & Mr. Richard B. Mellon
1930 Mr. George Eastman
1929 Mr. and Mrs. Francis P. Garvan
1927 Dr. Lafayette B. Mendel
1926 Dr. William Blum

Appendix B - Winners of The AIC Chemical Pioneers Award, 1966-2015

2014
Dr. Anthony Cheetham
Dr. Ann M. Valentine
Dr. Robert Langer

2013
Dr. Henry F. Schaefer, III
Dr. Tom Tritton

2012
Dr. Robert Lochhead
Dr. Helen Free

2011
Dr. James Christner

2010
Dr. Sossina M. Haile

2009
Dr. Keith Carron
Dr. Debashsi Mukherjee

2008
Dr. E. Gerald Meyer
Dr. Barnaby Munson

2007
Dr. Magid Abou-Gharbia
Dr. Dennis Y-M Lo
Dr. Alan G. Marshall

2006
Dr. David Devraj Kumar
Dr. Glenn Crosby

2005
Dr. C.N.R. Rao
Dr. Steven L. Suib
Dr. Bassam Shakhashiri

2004
Dr. Keki H. Gharda
Dr. Eric Jacobsen
Dr. Michael Pirrung

2002
Dr. Gérard Jaouen
Dr. Julius Rebek

2000
Dr. Richard A. Adams
Dr. Robert Bergman
Dr. Larry Dahl
Dr. Wilfried Mortier
Dr. Kenner Rice

1998
Dr. John E. Bercaw
Dr. Stephen J. Benkovic
Dr. Albert I. Myers

1997
Dr. Gregory R. Choppin
Dr. Attila E. Pavlath
Dr. Jerrold Meinwald
Dr. Murray Goodman

1996
Dr. William Hettinger, Jr.
Dr. George Keller
Dr. Fred McLafferty
Dr. Kyriacoc Nicolaou

1995
Dr. Ray Baughman
Dr. Ralph Parson
Dr. Gábor Somorjai
Dr. Owen Webster

1994
Dr. Norman L. Allinger
Dr. Frederick Hawthorne
Dr. John D. Roberts
Dr. Alan H. Cowley

1993
Dr. Derek H. R. Barton
Dr. Bruce Merrifield
Dr. George Olah ((Nobel Prize, 1994 Chemistry)
Dr. Jule A. Rabo

1992
Dr. Fred Basolo
Dr. Ralph F. Hirschmann
Dr. George W. Parshall
Dr. Gilbert Stork

1991
Dr. Michel Boudart
Dr. Edith M. Flanigen
Dr. Herbert S. Gutowsky
Dr. Jack Halpern

1990
Dr. Frank A. Cotton
Dr. Michael J. S. Dewar
Dr. James L. Dye
Dr. Paul G. Gassman

1989
Dr. Harry Allcock
Dr. Herman S. Block
Dr. David R. Bryant
Dr. Burton Christenson

1988
Dr. Frederick J. Karol
Dr. George R. Petit
Dr. K. Barry Sharpless
Dr. John H. Sinfelt
Dr. Robert C. West

1987
Dr. Federick E. Bailey
Dr. James Economy
Dr. Herbert S. Eleuterio
Dr. Daniel W. Fox

1986
Dr. Harry W. Cover
Dr. Robert D. Lundberg
Dr. James F. Rooth
Dr. Howard Zimmerman

1985
Mr. William Breneman
Dr. Alan S. Hay
Dr. Raymond Seymour
Dr. Otto Vogl

1984
Dr. Isabella L. Karle
Dr. Robert MacAllister
Dr. Alan G. MacDiarmid (Nobel Prize, 2000 Chemistry)
Dr. Ira E. Puddington

1983
Dr. Harry G. Drickamer
Dr. William S. Knowles (Nobel Prize, 2001 Chemistry)
Dr. Allen S. Russell
Dr. Barry M. Trost

1982
Dr. Alexander Mills
Dr. Herman Pines
Dr. Roy L. Pruett
Dr. Alfred Saffer

1981
Mr. Robert L. Banks
Dr. Elias James Corey (Nobel Prize, 1990 Chemistry)
Dr. Ralph Landau
Dr. Quentin F. Soper

1980
Dr. Paul H. Emmett
Dr. Denis Forster
Dr. Stephanie Kwolek
Dr. Robert M. Milton

1979
Dr. Karl P. Cohen
Dr. Paul Harteck
Dr. Barnett Rosenberg
Dr. Leo H. Sternbach
Dr. Alejandro Zaffaroni

1978
Dr. George E. F. Brewer
Dr. Karl Klager
Dr. Lewis G. MacDowell
Dr. John Patton

1977
Mr. John Kollar
Mr. Henry McGrath
Dr. Donald F. Othmer

1976
Dr. Rowland C. Hansford
Dr. Edwin T. Mertz
Dr. Wilson C. Reeves
Dr. Jerome S. Spevack

1975
Dr. Herbert C. Brown (Nobel Prize, 1979 Chemistry)
Dr. Rachel Brown
Dr. Elizabeth Hazen
Dr. Linus C. Pauling (Nobel Prize, 1954 Chemistry)
Dr. Christiaan Van Dijk

1974
Dr. Charles C. Hobbs
Dr. Samuel E. Home, Jr.
Dr. Charles J. Plank
Dr. Paul B. Weisz

1973
Dr. Melvin A. Cook
Dr. Carl Djerassi
Dr. Paul J. Flory (Nobel Prize, 1974 Chemistry)
Dr. Percival C. Keith
Dr. Bart Van't Riet

1972
Dr. Paul Hogan
Dr. Herman F. Mark
Dr. Alex G. Obla
Dr. E. Emmett Reid
Dr. Lewis Sarett

1971
Dr. C. Kenneth Banks
Dr. Oliver W. Burke, Jr.
Dr. Sterling Hendricks
Dr. Everett C. Hughes
Dr. Joseph H. Simons

1970
Dr. Gerald J. Cox
Dr. Tracy Hall
Dr. Foster D. Snell
Dr. William J. Sparks

1969
Dr. O.A. Battista
Dr. Irving E. Levine
Dr. Roy J. Plunkett
Dr. William Toland
Dr. Harold C. Urey (Nobel Prize, 1934 Chemistry)
Dr. Hervey H. Voge

1968
Dr. Ralph A. Connor
Dr. James D. Idol, Jr.
Dr. Glenn T. Seaborg (Nobel Prize, 1951 Chemistry)
Dr. Max Tishler

1967
Dr. Vladimir Haensel
Dr. William E. Hanford
Dr. Henry B. Hass
Dr. Carl S. Marvel
Dr. Benjamin Phillips
Dr. David W. Young

1966
Dr. Carl Barnes
Dr. Johan Bjoksten
Dr. Herman A. Bruson
Dr. Charles H. Fisher
Dr. Robert M. Joyce
Dr. Charles C. Price
Dr. Eugene G. Rochow

HOW TO REMOVE BIAS FROM PEER REVIEW

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(Originally appeared in The Chronicle of Higher Education, May 7, 2015. Reprinted with permission from Teri W. Odom.)

The ugly side of peer review was on full display last week when a scientific paper was rejected for reasons that smacked of sexism. Two female authors had submitted a paper to a journal that is part of the open-access PLOS family. A negative decision was made based on a single review stating, "It would probably also be beneficial to find one or two male biologists to work with (or at least obtain internal review from, but better yet as active co-authors). … "

The reviewer has since been removed from the PLOS reviewer database, and the editor was asked to resign from the editorial board. But the quandary concerning overt sexism — even misogyny — in academic journals remains.

In scientific journals, protection of peer-reviewer identity is a key tenet to ensure unbiased and fair assessment of the submitted work. In its best form, reviewers offer helpful critiques to improve the paper by pointing out possible errors in analysis, asking for more interpretation, or suggesting that other data is needed to fully support the findings.

Such candid comments are usually better received on paper than in person, which is why reviewer identity is protected. Abuse of this protection, however, allows reviewers free rein to provide their opinions, fair or not, about the work without facing consequences for inappropriate reviews or for needing to be responsible for their words.

Taken to an extreme, abuse of peer-review protection results in outcomes very similar to those of Internet trolls: Harmful comments can be made without recourse. Everyone knows anonymity breeds contempt.

I believe this unfortunate incident — which generated deserved outrage — is a failure of editorial leadership. The onus should not be simply on the reviewer.

As executive editor of ACS Photonics, part of ACS Publications, my role is to serve the scientific community by identifying expert reviewers, inviting them to offer unbiased and fair assessments of the submitted paper, and then making a decision based on those reviewer recommendations as well as my own reading of the paper.

To ensure consistency in the review process, typically two or more reviews are needed. What is critical to note is that although we invite reviewers to make recommendations on the paper (e.g. accept, revise, reject), it is the prerogative of the editor to actually make the decision.

In the unfortunate case above, editorial leadership was clearly missing. The editor should never have passed those comments along to the author, and there should have been more than a single, unsubstantiated review before a decision was made. And yes, that the editor stepped down from the editorial board was appropriate.

How Systemic is this Problem?

Although such data may be hard to come by, one significant change to the publishing landscape has been the rise of open-access journals. The idea behind these journals is appealing, where new scientific results can be made freely available to the public — and, indeed, there are some excellent ones.

However, the majority of open-access journals have focused on technically sound results of already reported findings, which may not necessarily translate to scientific impact. But the bigger challenge is that for many of these journals, the editorial process is not as rigorous, which, when unchecked, can result in the publication of papers on topics that are absurd or with no new content.

Editors of reputable scientific journals — practicing scientists and professional editors — have an obligation to ensure a fair review process and to protect authors from inappropriate and unsubstantiated comments. If editors are not held accountable, increased incidents of poor peer review and bias are bound to occur.

Early in my scientific career, I received a review that contained disparaging remarks such as my being "out of touch with modern developments" with "no elements of novelty … that could warrant publication … in any good journal." Even as I told my students not to take such remarks personally, it was hard not to. And, although this particular reviewer might write like this for everyone, the intent was clearly to harm the chance for possible publication (which worked, for that particular journal).

Perhaps a system of review for editors and reviewers would provide a check for demeaning comments. For example, if an editor fails to communicate that such commentary is not acceptable, then she or he should step down from that position. And if a reviewer makes outrageously biased comments more than once, then he or she would be barred from publishing in and reviewing for that family of journals.

Perhaps only then will it become common practice to concentrate on the science and the content, not the sexism.

NOTE: *Teri W. Odom is a Charles E. and Emma H. Morrison Professor of Chemistry at Northwestern University and the executive editor of* ACS Photonics.

SOAP BUBBLES: NOT JUST KIDS' STUFF!

David Devraj Kumar
Florida Atlantic University | Davie, FL 33314

What are Soap Bubbles?

Soap bubbles are part of our life, so often we ignore them. Kids play with them, so it's kids' stuff! In fact, soap bubbles have drawn the attention not only of children but also of chemists, physicists and mathematicians, some as great as Sir Isaac Newton.

Soap bubbles are formed when air is trapped inside soap films, sandwiching a thin layer of water between two layers of soap molecules. The polar oxygen-rich hydrophilic end of the soap molecule is attached to water molecule and the nonpolar hydrocarbon chain hydrophobic end repels water (Katz, 2010; Pepling, 2003). Due to the presence of two layers of soap films, light gets reflected off the outer layer and the inner layer leading to constructive and destructive interference. Depending upon the thickness of the soap bubble and the angle of the incident light, soap bubbles display various colors. Sir Isaac Newton studied the interference colors of thin films and made calculations of thin film thickness (Hall, n.d.). He calculated the thickness of soap bubbles at their thinnest point to be 1/2500000 inch or 0.000001016 centimeter.

Soap Bubbles and Weather Systems

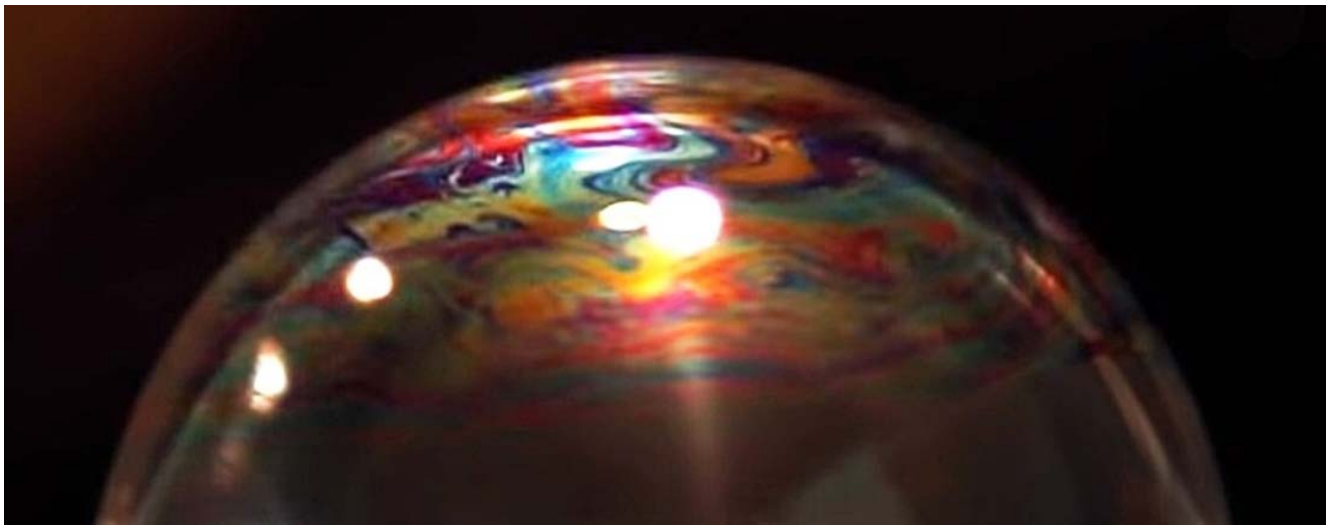

Fig 1. Surface currents on a soap bubble.

One of the recent developments involving soap bubbles is not only high tech but also significant in terms of its impact on our ability to understand extremely complex tropical weather systems. Researchers have shown that upon heating, soap bubbles generate (Gaussian) vortices and convection currents similar to those naturally occurring in hurricanes and typhoons (Seychelles, Amarouchene, Bessafi, and Kellay 2008; Meuel, Xiong, Fischer, Bruneau, Bessafi, & Kellay, 2013). The variations in thickness at different points of the soap bubble, due to temperature variations, generate surface currents in the bubble similar to atmospheric currents, in addition to producing color displays (Figure 1).

The color displays make it easier to follow the surface currents. Comparison of data from soap bubble-created simulated hurricane systems to data from real hurricanes has shown encouraging similarities supporting the use of soap bubbles as experimental models for understanding weather systems.

Something to Think About

As noted earlier, it is quite amazing indeed how a simple soap bubble formed by trapped air inside a skin of thin layer of water molecules sandwiched between soap molecules is providing a dependable system to study complex weather systems. Chemistry goes beyond test tubes in chemistry laboratories and boring chemistry lectures in chemistry departments. Whether one knows it or not, soap bubbles bring chemical science to real life. Even meteorologists take soap bubbles seriously. So, next time you see a soap bubble, don't just ignore it as kids' stuff.

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ACKNOLEDGMENT: Figure 1 Source - D. Cowern. How to make a hurricane on a bubble. *Physics Girl*. https://www.youtube.com/watch?v=nXDKCm2dfMs. Used with permission.

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.

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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.

- **Journals -** The general format for citations should be in the order: **author(s), journal, year, volume, page**. Page number ranges are preferred over single values, but either format is acceptable. Where page numbers are not yet known, articles may be cited by DOI (Digital Object Identifier). For example:

  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.

- For material accepted for publication, but not yet published, the following form should be used:

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

- For material submitted for publication but not yet accepted the following form should be used:

  Jones AB, *Anal. Chem*. submitted for publication.

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