Parylene Conformal Coating improves Medical Devices

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This examination of the characteristics, performance and application of Parylene conformal coating will cover issues related to its use to isolate and protect medical substrates. Parylene, a conformal polymer film, is now quickly finding more applications in Europe. Benefits are environmental and dielectric isolation in a variety of applications. The most important performance specifications for a conformal coating are its uniformity and completeness of coverage and its physical, electrical, chemical, mechanical and barrier properties. Parylene is not affected by volatile organic compound restrictions. As a transparent and flexible film, Parylene meets with requirements of a USP Class VI plastic and is applied as a film in layers as thin as 0.5 microns to provide pinhole-free coating. Applications that will be discussed include catheters, mandrels, pacemakers, cannulae, electronic circuits, pressure sensors and metal parts and packaging.

Coating Characteristics

The poly-para-xylylenes (" Parylene" in short) are members of a family of thermoplastic polymers that are formed on surfaces by an active monomer gas rather than being applied as a liquid by conventional coating methods. This application process has several useful features. Such as:

1. *It is effective in very thin layers* - for example, 2-10 microns of thickness is ample for protection of pacemakers and stents.

2. *Parylene application is at room temperature*. The Parylene polymerisation process uses no solvents or additives. There is no outgassing, and no differential cure forces to act on fragile components or coated substrates.

3. *Parylene is inert*, and highly resistive to moisture, hydrocarbons, acids and other agents.

4. *Parylene is applied as a gas rather than a liquid*, making it highly Conformal to the surfaces of coated assemblies. Encapsulation is complete and free of pinholes and

coating gaps. Parylene film has essentially no undesirable physical or mechanical impact on underlying surfaces, even with wide temperature excursions. In contrast, liquid coatings form a dimensional structure that can exert unwanted mechanical force on underlying surfaces -- both during cure, and with thermal cycling over the life of the substrate.

The Parylene Coating Process

In a previous paper (Ref.1) the Parylene deposition process was described and it's applications summarised. This paper focuses on recent issues issue related to permeability of water and gasses, which are often of first consideration when considering a coating at all.

Vacuum deposited Parylene is applied in an evacuated chamber by means of gas phase polymerisation. The coating grows (at ambient temperature) from the substrate surface outward, and thus its thickness is infinitely controllable from as little as 100 Angstroms to over 75 microns. As a result, users can obtain the required protection with minimal coating mass. Since there is no cure cycle with Parylene, substrates are not subject to cure forces, solvents, liquid phase or elevated temperatures, and no testing is required to confirm that full cure has occurred.

Poly-para-xylylene Versions

There are three common forms of the Parylene polymer: Parylene C, Parylene N, and Parylene D. Each has unique properties that suit it to particular coating applications.

For example, Parylene N has particularly high dielectric strength, with the ability to coat deep recesses and blind holes. Parylene C has low permeability to moisture and corrosive gases. The Parylene C's deposition rate is substantially faster than Parylene N, and its crevice penetration is thereby reduced. Parylene D, the highest degree of thermal stability of the three Parylenes.

Dry film lubricity is a useful attribute in some Conformal coating applications. Parylene static and dynamic coefficients of friction are in the range of 0.25 to 0.33, making this coating equivalent to Teflon® .

Parylene Permeability Properties for Medical Coating

A commonly asked question relates to the difficulty in interpreting data on permeability of water vapour and other gasses through polymer films , such as Parylene. See Appendix 1 for details. Summarising standardised literature, it can be understood why the Parylene polymers are so successful in improving medical devices. The permeability of especially Parylene C is lower than almost any other engineering plastic. See Table.1

Table 1 Normalised permeability of gasses through polymer materials.

H2O in cm3.mm/m2.day.atm. All gasses in g.mm/m2.day Ref.12.

	O2	N2	CO2	H2	H20
Parylene C	2.8	0.4	3	43	0.08
Parylene D	12	1.8	5	94	0.1
Parylene N	15	3	84	213	0.6
HDPE	73	17	228	n.d.	0.12
PS	138	23	400	n.d.	3.5
PTFE	223	133	n.d.	516	n.d
LDPE	140	80	700	n.d.	0.6
PC	124	22	827	n.d.	1.5
FEP	295	126	657	381	0.16
Silicone	19000	n.d	118000	17000	3

Foreign objects or materials that come into direct and prolonged contact with human body tissues in the course of medical procedures must be compatible and have long term resistance to components such as corrosive body fluids, electrolytes, proteins, enzymes and lipids.

Protective Conformal coating of a biomedical surface may be required for one or more reasons. These include:

- physical isolation from moisture, chemicals and other substances
- surface passivation
- electrical insulation

- locking and immobilisation of microscopic particles
- and friction reduction.

A vacuum-deposited Parylene film of controllable thickness can satisfy these and other surface treatment requirements.

Chemical inertness is a crucial issue for producers of medical implants and surgical components, where mechanical performance requirements may be at odds with biostability issues.

Medical materials that are not intrinsically biostable must be protectively coated using an isolating material and a process that does not degrade their functionality, including preserving mechanical tolerances and critical performance characteristics.

For example, bone pins and prosthetic hardware, catheters, cardiac pacemakers, needles, medical probes, and Cochlear implants must be biostable to avoid substrate degradation and compromise of medical efficacy. Of special interest at present is Parylene and cardiovascular stents. As the Industry alert on stents CBS 671 prepared by Clinica in 1996 indicated the market for coatings is growing. Ref. 11

Reasons for coatings on stents are twofold; to prevent thrombosis and to realise a reduction of neointimal hyperplasia (growth of the internal artery vessel wall as a result of an angioplasty procedure). Coatings either improve surface effects of stents or provide pharmaceutical effects. This can be obtained by a permanent coating on the surface or by eluting a drug into the vessels wall. Hence coatings can be either passive, active or drug eluting.

Passive coatings modify the surface of stents to reduce immediate thrombogenecity or increase long term biocompatibility. Active coatings include materials which have a pharmacological effect but do not elute a drug into the tissue surrounding the stent. Eluting coatings are designed to release drugs into the micro-environment of the stent.

Examples of passive coatings are Phosphorcholine Amorphous Silicon-carbide and Biogold. Active coatings are non-eluting heparin and polyurethane-heparin co-deposited mixtures. Drug eluting coatings are Dexamethazone , Hirudin and RGD-peptide . Parylene itself has to be ranked in the first category, and is used on pacemakers, stents and Cochlear implants.

Parylene clearly is a passive coating, with the advantage that it is a Conformal polymer film that provides environmental and dielectric isolation in a variety of applications, including various medical substrates, electronic circuits, industrial and automotive sensors, and archival preservation of documents and archaeological samples.

As a non-solvent based coating, Parylene is not affected by volatile organic compound (VOC) restrictions, and it is not implicated in the ozone depletion concerns of the Montreal Protocol and other environmental legislation.

Traditional Conformal coatings are solvent-based liquid resins or sputtered coatings. Some liquid coatings are also available in 100 percent solids form without solvents. All such materials exhibit properties (pooling, meniscus, etc.) that may make them unsuitable for some medical coating applications as they are not pinhole free. Additionally, new coatings may not meet toxicity and/or biocompatibility requirements, and can require extensive random clinical trials .

Transparent and flexible Parylene is covered by FDA Parylene master drug file MF 1825. Also a medical device File No. MAF 263 is kept. The coating meets the requirements of a USP XXI Class VI plastic, and can be applied as a film in layers as thin as 0.5 micron to provide pinhole free and Conformal coverage, even on complex surfaces.

Parylene has been shown to be highly resistant to the potentially damaging effects of corrosive body fluids, electrolytes, proteins, enzymes and lipids. Ref.

2,3.The film also forms an effective barrier against passage of contaminants from a coated substrate to the body or surrounding environment. This chart lists gas permeability values for the Parylenes as well as typical values for other coating materials. Ref. 2,3,4,5.

The conversion from monomer gas to polymer film is direct, and there are no solvents, plasticizers, catalysts or accelerants. The resulting film has very low thrombogenic properties and low potential to trigger an immune response.

This protective film resists chemical attack from organic solvents, inorganic reagents, and acids, has good adherence to plastics, ceramics, glasses, and metals. Devices coated in this manner may be sterilised with steam, ETO, paracetic acid, or radiation. Ref. 6,7,8,9.

The Parylene Conformal coating process offers unique benefits for selected medical applications including:

- dry film lubricity
- particle immobilisation
- hydrophobicity, biocompatibility
- chemical insolubility
- freedom from by-products
- immunity to hydrolytic degradation
- thermal stability
- low permeability
- and high electrical resistivity.

The demands of medical coating are varied and critical, and depend on the form and function of the substrate. In some cases, these requirements cannot be met with conventional liquid coatings. For example:

- **Cannulae** require application of dielectric insulation and with precise thickness control.
- **Silicone seals** demand lubricity and inertness along with minimum change to dimension and durometer values.
- **Catheters** need lubricity and inertness, and consistent coating thickness over widely varying geometry.
- **Stents** require biocompatible surface protection with absolutely minimal impact on dimensions and physical or mechanical properties of complex topographies.
- **Blood pressure transducers** require precise coating thickness across their 1 to 2 mm dimension.

APPLICATION	PARYLENE N	PARYLENE C
Catheter Mandrels	Lubricity	
Feeder Tubes	Crevice Penetration	
Laproscopic Devices		Dielectric Strength
Animal Identification		Barrier Properties
Catheters/Stylettes		Lubricity
Cardiac Assist Devices		Barrier/Dielectric
Orthopaedic Hardware		Biocompat. Barrier
Pressure Sensors		Dielectric/Barrier
Prosthetic Components		Barrier/Lubricity
Stents		Biocompat. Barrier
Electronic Circuits		Dielectric/Barrier
Ultrasonic Transducers		Biocompat. Barrier
Bone Growth Stimulators		Biocompat. Barrier
Cochlear Ear Implants		Barrier/Dielectric
Brain Probes		Biostability
Blood Handling Components		Biostability
Needles		Biostability
Cannulae		Biostability
Bone Pins		Biostability
Analytical Lab Trays		Biostability

Table 2 - Primary Parylene coating functions for selected medical substrates.

The most common Parylene medical coating applications are summarised by Parylene type in this table 2.. In general, Parylene N is selected where lubricity and high crevice

penetration are required. Parylene C is appropriate to most medical coating applications because of its moisture barrier properties, gas low permeability, and best overall performance. (Parylene D is generally limited to industrial applications where thermal stability and mechanical toughness are of greatest importance.)

The dry film lubrication properties of Parylene also complement prosthetic components such as bone pins and artificial joints. Parylene coating of screws and nuts used with temporary bone pins and plates can prevent seizing, corrosion, and metal fragmentation. The hydrophobic and lubricious nature of Parylene coating can minimise residual fluid build-up on both inner and outer surfaces of needles and other medical components, thus aiding cleanup. Parylene is especially effective in sealing the microporosity of metals that could otherwise trap and retain contaminants.

Data on the body tissue and blood compatibility (Ref. 4.)of Parylene have been obtained in studies in several US based institutes such as at Battelle Memorial Institute, University of North Carolina, Johns Hopkins Hospital, University of California (San Diego), Carnegie Mellon University, University of Michigan, and several other institutions. Ref. .5,6,8. In experiments by the US National Heart, Lung and Blood Institutes inert Parylene has been used to coat and anchor experimental fabrics used as linings for circulatory assist devices. In vitro tissue culture studies show that human cell types (e.g., Chang liver cells, Wish amnion cells), as well as bovine and ovine fibroblasts, readily proliferate on Parylene coated surfaces to produce thin, adherent layers of morphologically normal tissue. Further, deposition of a thin film of Parylene over a toxic surface has been shown to render it atraumatic to cells.

Parylene C polymer has been evaluated in blood compatibility tests at the University of North Carolina. In these in vitro tests it ranked thirteenth among fifty-seven materials. Among materials ranked significantly lower are polyhydroxyethyl methacrylate, TFE and FEB fluorinated polymers, polydimethylsiloxane, and polyvinylpyrrolidone. Stypven and partial thromboplastin times were employed to

measure thrombogenic activity. Haemoglobin and adenine nucleotide release were also measured.

Parylene polymers will continue to find increased usage in critical biomedical applications because of it's : (1) extreme inertness and purity of the end product makes the Parylenes a logical choice in both functional and safety aspects; and (2) unique ability to form these polymers from a molecular state would seem to indicate that the Parylenes will be the only coating technology able to address the increasing complexity and shrinking geometry of the rapidly- evolving medical device field.

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APPENDIX Permeability of Water in Parylene C

In order to understand the permeability coefficient for water in Parylene C, P = 2.05×10^{-9} scc·cm/cm^2·day·cm Hg, calculated in "Determination of the Water Vapour Permeability and Continuity of Ultrathin Parylene Membranes" J. Electrochemical Soc. 119 (11) 1592-1594 (1969), we should start by recalling the following basic points:

1. The partial pressure of water at 23°C and 100% Relative Humidity is equal to the vapour pressure of water p^0 at 23°C, or 21.08 mm Hg.

   Here is a table of the vapour pressure of water at a few specific temperatures:

T, °C	0	20	23	25	30	37	50
p^0, mm Hg	4.58	17.54	21.08	23.76	31.84	47.10	92.5

1. 1 mole of water = 18.015 grams.

2. 1 mole of an ideal gas occupies 22.4 litres at standard temperature and pressure (STP) (p = 1 atmosphere, T = 0°C).
3. Hence 1 scc (one standard cubic centimetre = 1 cm^3(STP)) of water =

$$= \frac{18.015 \text{ grams / mole}}{22400 \text{ scc / mole}} = 0.8042 \text{ mg of water.}$$

In the above referenced ECS article, the area of the opening of the "Payne Cup", over the mouth of which the Parylene film adheres during the permeation measurements, is not given. This is no doubt an oversight, but without it we can't calculate a Permeability from the data given. However, by assuming a value for area of the membrane which results in a best agreement with the Permeability results given in the

ECS article, we can make a guess at what the authors neglected to include. Below is a reprocessing of their data.

Q0, g/day,=0.3873 A,cm2,=4.34 2.35=R,cm

Qinf, g/day,=0.0010 po,cm Hg,=2.108

Thickness	Qobs	Qf	Permeance	Grad P	P (calculated)	P (reported)
Angstroms	g/day	g/day	scc/s/cm2	Cm Hg/cm	10-9 scc-cm/cm2-s-cm Hg	
292	0.2207	0.5077	1.68E-03	721918	2.33	2.38
836	0.1091	0.1500	4.97E-04	252153	1.97	1.97
1946	0.0529	0.0599	1.99E-04	108325	1.83	1.83
3701	0.0308	0.0323	1.07E-04	56958	1.88	1.87
6080	0.0207	0.0208	6.88E-05	34671	1.98	1.98
7470	0.0179	0.0177	5.86E-05	28220	2.08	2.08
11069	0.0136	0.0130	4.32E-05	19044	2.27	2.27
23100	0.0064	0.0055	1.82E-05	9126	1.99	1.98
78388	0.0027	0.0017	5.66E-06	2689	2.10	2.06

The Q_{obs} are the observed rates of weight loss with Parylene C films of various thicknesses adhered across the mouth of the cup, uncorrected for the weight loss by serial and parallel processes which will be discussed later. From the corrected weight loss rates, Q_f, by dividing by the area of the mouth of the cup and therefore of the film secured across it and adjusting time units, we get a Permeance for the film in scc per second per cm^2 of area of the film. The area which leads to the best fit with the results reported in the ECS paper is 4.34 cm^2, corresponding to a circular opening of 2.35 cm diameter, or a little less than one inch.

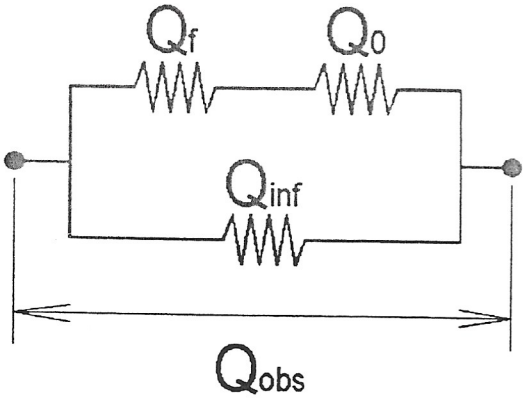
flows through it per unit area, under a specific set of conditions†. Permeance should vary directly with the driving force for the permeation, the pressure gradient across the film. In fact, the ratio of Permeance to the pressure gradient across a homogeneous film or membrane gives the Permeability of the material of which it is made. In the work described in the ECS paper, there was an attempt to assure that the dry side of the film had negligible partial pressure of water by the use of desiccants, so that we have reason to hope that the pressure gradient across the film is as much as the vapour pressure of water, 21.08 mm Hg at 23°C, divided by the thickness of the film.

ASTM E96 is the Standard Test Methods for Water Vapour Transmission of Materials document. It recommends a test area of 30 cm^2 or more, as opposed to the 4.34 cm^2 used here. However, E96 addresses the problems of measuring WVT in samples up to 1/8" thick, and the Parylene C films we deal with here are at or below the range for which E96 is intended. Since the authors seem to have had adequate sensitivity for the job at hand, the employment of the smaller area is probably acceptable. E96, in the version dated 1980 which I have easy access to, gives us no help in understanding what a "Payne Cup" might be.

Finally, it will be useful to devote a little more attention to the corrections made for parallel and serial conductances within the MVT testing equipment. The authors allude to an electrical conductance analogue, and presume the reader will follow. For those among us who wish they were more nimble with electrical circuit calculations, here's what the authors meant. The MVT test apparatus can be represented by analogy as the resistor network pictured to the right. Just as electrical resistance and electrical conductance have a mutual reciprocal relationship (R = 1/Q and Q = 1/R), so analogously does water transport conductance and resistance in the test equipment. The conductance Q_f is the conductance we desire, that of the film under test, and Q_{obs} is the conductance we measure. All conductances are expressed in units of grams of water transported per day. A conductance Q_0 in series with the film conductance

† The term Permeance as used here differs from the use of the term "water vapor permeance" of

arises as a result of the need to transport water vapour across the open spaces of air between the liquid water on one side of the film and the desiccant on the other. It is expected to depend heavily on the exact geometry of the test equipment. Another conductance $Q_{inf} = Q_{\infty}$ exists in parallel with the film, the result in this equipment of a sidearm bleed necessary to equalise total pressure across the film. These two conductances can be evaluated by measuring Q_{obs} on an open cup and a cup closed with a film known to have zero conductance, and in fact values for these quantities appear in table 1 of the ECS paper.



Recalling that conductances add in parallel while resistance add in series, we can immediately write down an expression for Q_{obs} as a result of the resistive model diagrammed above:

$$Q_{obs} = Q_{inf} + \frac{1}{1/Q_f + 1/Q_0}$$

When this expression is solved for Q_f, we arrive at precisely the expression given as equation 2 in the ECS paper:

ASTM E96.

$$Q_f = \frac{Q_0(Q_{obs} - Q_{inf})}{Q_0 + Q_{inf} - Q_{obs}}$$

From this latter equation, we learn by inspection that when $Q_f = 0$ (infinitely thick film (aluminium foil) on cup, zero permeation), $Q_{obs} = Q_{inf}$. And when $Q_f = \infty$ (no film, open cup), $Q_{obs} = Q_0 + Q_{inf}$. We have no reason to doubt that the authors used these relationships to interpret the open cup and aluminium foil experimental data in producing the Q_0 and Q_{inf} which they list in the table 1.

Based on discussion With Dr. William F Beach.