A special polymer film, developed at the Institute of Physical Chemistry of the Polish Academy of Sciences in Warsaw, recognizes molecules of neopterin. The film is a key element of future cancer detectors. Credit: IPC PAS, Grzegorz Krzyzewski
Many cancers could be successfully treated if the patient consulted a doctor sufficiently early. But how can a developing cancer be detected if it doesn't cause any symptoms? In the near future, suitably early diagnosis could be possible via cheap, simple chemical sensors, thanks to chemosensing polymer films developed at the Institute of Physical Chemistry of the Polish Academy of Sciences in Warsaw.

These days, cancer is no longer a death sentence. However, early treatment confers the best chance of recovery. Timing is the problem, because many tumours develop over a long period without symptoms. One solution could be home diagnostic tests that could be performed by consumers on a relatively regular basis. A chemical sensor devised and fabricated by scientists at the Polish Academy of Sciences (IPC PAS) in Warsaw brings such chemosensing diagnostic tests closer.

The most important element of the chemosensor is a thin polymer film that detects molecules of neopterin, known in chemical terminology as 2-amino-6-(1,2,3-trihydroxypropyl)-1H-pteridin-4-one). Neopterin is an aromatic compound present in human body fluids such as blood, serum, urine, and cerebrospinal fluid. Produced by the immune system, it is regarded as a universal marker in medical diagnosis. The concentration of this biomarker rises significantly in the case of certain neoplastic diseases like malignant lymphoma, although elevated levels of neopterin are also seen in some viral and bacterial infections, as well as in diseases of parasitic aetiology. In transplant patients, increased levels of neopterin signal probable rejection.

"How can we detect the presence of neopterin? A reasonable approach is to use special recognizing materials for this purpose, prepared by molecular imprinting. This technique involves 'stamping out' molecules of the desired compound—their shape, but also at least some of the chemical characteristics—in a carefully designed polymer," explains Dr. Piyush Sindhu Sharma (IPC PAS), the lead author of an article
published in the *Biosensors and Bioelectronics* journal.
A special polymer film, developed at the Institute of Physical Chemistry of the Polish Academy of Sciences in Warsaw, recognizes molecules of neopterin. The film is a key element of future cancer detectors. Pictured above: Dr. Piyush Sindhu Sharma in the IPC PAS laboratory. Credit: IPC PAS, Grzegorz Krzyzewski

During the preparation of the polymer film, molecules of the target substance—in this case neopterin—are suspended in a working solution in which their binding sites have to link with recognizing sites of so-called functional monomers. In turn, these monomers should be able to form connections with another monomer, a cross-linking agent. Together, after polymerization, these constituents form the rigid support structure of the polymer. Next, the neopterin molecules used as a template are washed out of the structure. The result is a durable polymer with molecular cavities which have the shape and chemical properties to ensure the capture of neopterin molecules from its surroundings.

The basic difficulty in molecular imprinting is the selection of the appropriate functional and cross-linking monomers and solvents, and determining their proportions and reaction conditions. Ph.D. student Agnieszka Wojnarowicz (IPC PAS) explains: "With the aid of quantum-chemical calculations, we first check whether there is bonding between our template molecule and selected functional monomers, and whether they will be stable in the solvent used. We also check whether the molecular cavities formed are sufficiently selective—i.e., whether they will primarily capture the molecules we are detecting, and not any that are similar to them. When the calculation results confirm our expectations, that is when we proceed to their experimental confirmation."
At the IPC PAS a recognizing polymer film with molecular cavities from neopterin has been produced on the surface of an electrode. After immersion in artificial blood serum spiked with neopterin, the film on the electrode captured neopterin molecules, thus leading to a decrease in electrical potential in the connected measuring system. The tests showed that the molecular cavities of the polymer were almost entirely filled with molecules of neopterin despite the presence of molecules of similar structure and properties. This result means that the probability of false positive detection is negligibly small. The new chemical sensor therefore mainly reacts to what it should react to and nothing else.

"At present, our chemosensor is a piece of laboratory equipment. However, the production of its key element, that is, the recognizing polymer film, does not pose major problems, and the electronics responsible for electrical measurements can easily be miniaturized. There is nothing standing in the way of building simple and reliable diagnostic equipment, based on our development, in just a few years' time, which would be affordable not only for medical institutions and doctors' surgeries, but also for the public in general," predicts Prof. Kutner (IPC PAS).


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