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Lab-On-a-Chip an integrated microfluidic device sensitive low-Cost, and Rapid with a syringe pump for Analysis of Ibuprofen

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Abstract: Microfluidic devices present unique advantages for the development of efficient drug assay and screening. The microfluidic platforms might offer a more rapid and cost-effective alternative. Fluids are confined in devices that have a significant dimension on the micrometer scale. Due to this extreme confinement, the volumes used for drug assays are tiny (milliliters to femtoliters).

In this research, a microfluidic chip consists of micro-channels carved on substrate materials built by using Acrylic (Polymethyl Methacrylate, PMMA) chip was designed using a Carbon Dioxide (CO_2) laser machine. The CO2 parameters have influence on the width, depth, roughness of the chip. In order to have regular channel surface, and low roughness the laser power (60 W), with scanning speed (250 m/s) for allows us to obtain microchannels with a minimum diameter of width (450 µm), depth of the channels was 89.4 µm and(Arithmetic Average Roughness Ra = 2.3), (Relative roughness, Ɛ = 5%) surface roughness with high accuracy and good surface quality.

The functionalized multiwalled carbon nanotubes (F-MWCNTs) was used to enhance the drug signal inorder to detect very tiny Ibuprofen concentration. In this work, laser microfluidic sensor have high accuracy in Ibuprofen detection compared to the traditional method(UV-VIS) spectrophotometer with LOD equal to 0.**25** nM, 1000µM respectively.

Keywords: microfluidic chip, syringe pump, acrylic, Ibuprofen, grbl laser program, diode laser (532m).

Introduction

Microfluidics is a field of science studying fluids (i.e., liquids and gasses) on a microscopic scale. Therefore, fluids are confined in devices that have a significant dimension (e.g., the height or the width) on the micrometer scale[1-4]. Due to this extreme confinement, the volumes used for drug assays and similar studies are tiny (milliliters to femtoliters), and special physics apply. In short, in a microfluidic device there are only laminar flows and no turbulences, which grants an extremely high control over the fluids employed, diffusion of drugs and the progress of reactions [5-9]. Several types of microfluidic penetrate into these micro channels, and then some of these fluids are stored in the micro channels. Then, these fluids are combined with the mixers and create a specific reaction. Finally, the final product of this reaction will come out of the machine. The function of this device can be checked by ultraviolet microscopes, etc. Microfluidic systems have vast applications that have widespread use of the system in medicine and biology, as well as in research and laboratory. The technology of lab on a chip (LOC) is one of the applications of these systems that part of the chip acts as a part of the lab. The benefits of this technology include high sensitivity, isolation, reduced time and cost, high reparability and excellent detection[10-13]. Materials of the Chip Silicon and glass are the

earliest substrate materials used in microfluidic chips, mainly because they can directly use processing methods in the field of MEMS and microelectronics. Silicon and glass materials are expensive and difficult to process, which have been replaced by a variety of low-cost polymer materials, such as elastomer materials [14], thermoplastic polymers [15], thermosetting polymers [16], paper materials [17], biomaterials [18], etc. In this paper, the materials used for low cost microfluidic chip fabrication are polymer materials.

Polymeric microfluidic devices have the potential to overcome these drawbacks, offering advantages of economy and ease of fabrication[19]. Poly (methyl methacrylate) (PMMA) has been seen as viable alternative, due to its good optical and dielectric properties, low glass transition temperature, ease of processing [20]. Ibuprofen, 2-(4-isobutylphenyl)-propionic acid [15687-27-1], is non-steroidal anti-inflammatory drug that is available in a variety of preparations[21]. It is commonly used in treatment of pain and inflammation in rheumatoid arthritis and other musculoskeletal disorders. Several methods have been reported for the determination of ibuprofen in pharmaceutical samples and biological fluids, including HPLC,gas chromatography–mass spectrometry , capillary electrophoresis , spectrophotometry and spectrofluorimetry[22]. Clinically, it is safe and effective for Antipyretic, although the analgesic effect is stronger than aspirin, Phenyl butazone or acetaminophen, but the mechanism of anti-inflammatory and analgesic effect has not been completely clarified. one of the common skin reactions in the side effects of ibuprofen is itching, occasionally ulceration and bleeding and skin rash, and stimulation to the gastrointestinal tract [23]. The efficacy of constructed laser microfluidic sensor fabricated by CNC machine to determine Ibuprofen are discussed in this work. The influence of F-MWCNTs on the determination of the LOD of ibuprofen is presented and compared with determination of IB using UV-VIS spectrophotometer.

2. Materials and method

2.1. Design& Fabrication of laser Microfluidic system

Microfluidic system with two input channels and one output. Following modeling, micro-channel design, infusion pressure optimization, and time control are investigated. A two-channel microfluidic design was built by using polymer (PMMA).
The microfluidic chip design was created using Solid works. The layout of the microfluidic chip is show in figure (1a). The microfluidic consists of two inlets and one outlet. PMMA was fabricated by CO_2 laser. Two PMMA layers were manufactured with a thickness of 2mm a measure (2 cm* 5 cm). The first layer contains two inlets and one outlet. The second layer is the implementation of the design of the wafer shape by laser. The end picture of the microfluidic chip is shown in figure (b).

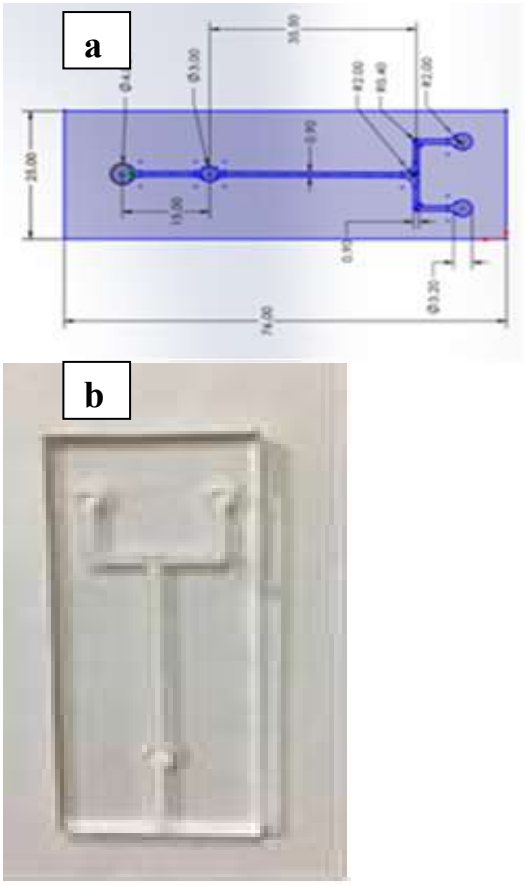


Fig. 1: Two Channel Microfluidic Channel Design. (a) Design by Solid works thickness 2mm. (b) The end picture of the microfluidic chip.

All PMMA,samples after microchannel fabrication then cleaned and washed with DI water to get rid of polymer residues. A digital microscope with (Hitachi, Tokyo, Japan) was used to measure the width. Images were taken under.10 X focal length. Also confocal,laser scanning microscope,(Image -pro Plus 6.0: Media Cyberneyics, Washington Dc,USA) was used,to measure the depth and Surface

roughness of the channel. The fabrication process of the PMMA based microfluidic chips. Thirdly, the PMMA substrate, was been covered with an epoxy resin used as an adhesives, then the PMMA
substrate was attached to another layer of PMMA,(same material and same thickness) containing holes (Two inlets,and one outlet), finally, to seal off the manufactured microchannels. The pipes for inlets and outlet ports then connected to the holes to finish the fabrication process.of the microfluidic chip.
Inlets, and one outlet), finally, to seal off the. manufactured microchannels. The pipes for inlets and outlet ports then connected to the holes to finish the fabrication process.of the microfluidic chip.

The construction of the syringe pump system needed electrical and mechanical engineering. Colorful models and circuits were estimated in order to find the stylish design for the below reasons. The custom corridor for the injection pump were created using SolidWorks design software. Cura software was used in 3D printing test models of designs on a regular direct printer. In order to produce completely cohesive pieces, accurate measures were needed. Figure (2a) shows the Solid Work assembly of a single syringe pump model with all corridors planned. The first type was put through its paces to insure it had a solid frame and moved easily. Figure2 (b) depicts the picture of the fabricated syringe pump.

Figure (3) shows the constructed laser microfluidic sensor, which consist of diode laser(532nm,20 mW),lens) focal length 1.5 mm),detector from UNO, Gentec, PH100 & PH20 series, china, fabricated double syringe pump to provide the pumping of F-MWCNTs and Ibuprofen ,microfluidic chip and PC. In this sensor the standard solution of Ibuprofen.

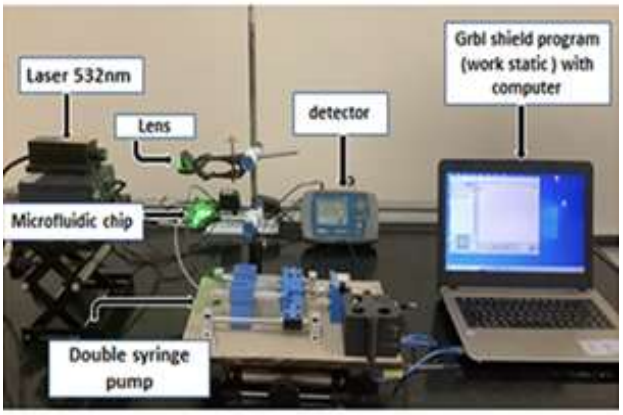


Fig. 3: Set up of laser microfluidic sensor

2.2. Standard solutions

Stock solutions of 1 mg/ml of IB were prepared by dissolving 100 mg of IB in 100 ml water. The solutions were prepared by dilution of the stock solutions with the same solvent to reach concentration range (250, 500,1000, 4000, 7000, 9000) μM.

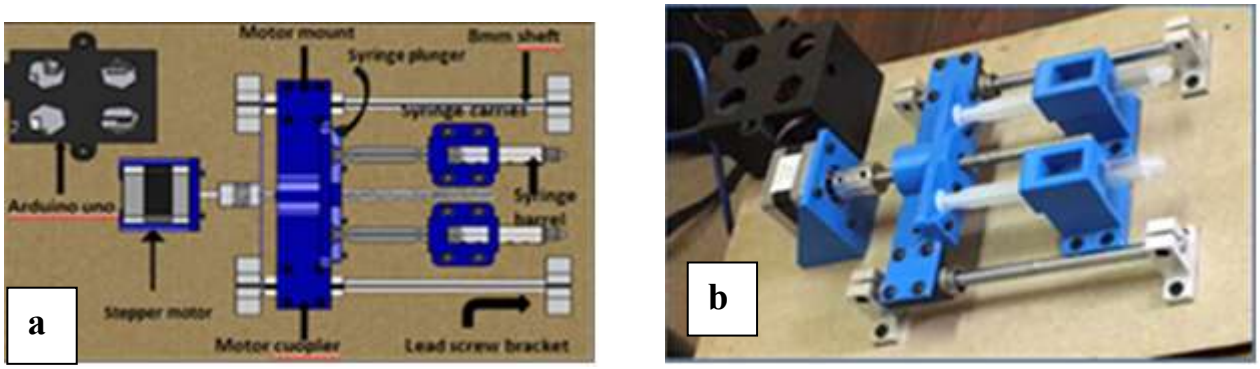


Fig. 2: (a) Solid Works design software 3D model assembly of a double syringe pump (b) fabricated syringe pump assembled with Nema 17 motor and 5mL syringe

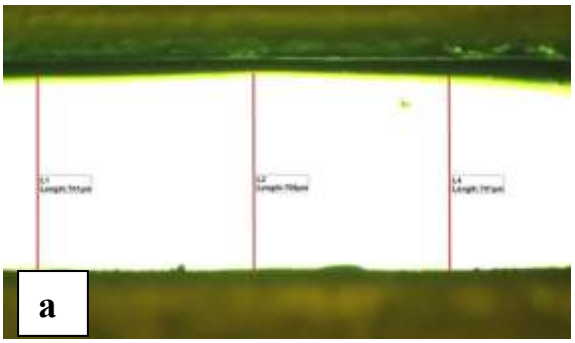
3. Result and Discussion

3.1. Characterization of Microfluidics Chip

In Figure 4(a), microscope images of the microfluidic chip fabricated by laser ablation. Channels produced using laser ablation exhibited a regular shape and clean ablation edge. The channel width 450 µm with associated uneven topography. Since PMMA has a relatively low thermal diffusivity, the intensity distribution mostly defines the channel profile. The microchannel has a Gaussian-shaped profile as a result of laser beam's energy being distributed Gaussianly.

A pool of molten polymer is formed on the workpiece surface where the laser beam makes contact with it as it advances over the surface. The heated gas of the vaporizing polymers drives the pool away from the hot point in all directions, while the majority of the melted material re-solidifies in the aftermath of the beam, leaving behind minor bumps on the microchannel's borders. The surface roughness of the laser ablated microfluidic chips was also measured with the help of the laser confocal microscope. Figure3(b) shows the laser confocal microscope image of the laser-ablated microchannel with a laser power of 60 watt and a travel speed of 250mm⁄s. The surface roughness was measured at the inner wall of the fabricated microchannels (Arithmetic Average Roughness Ra = 2.3), (Relative roughness, Ɛ = 5%) surface roughness with high accuracy and good surface quality.

Also, the laser confocal microscope used to find the depth of the channels which is equal to 89.4µm.



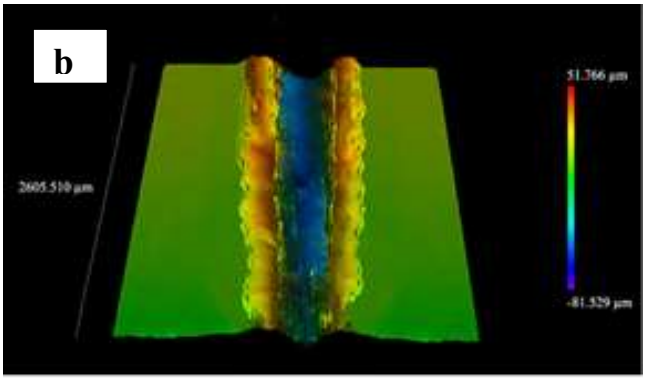


Fig. 4: (a) Showing width of the microfluidic chips via the optical microscope images at power of laser is constant at 60watt &travel speed is 250 mm/s (b) Showing the depth of the microfluidic chips via Confocal Laser Scanning Microscope.

3.2. Determination of Ibuprofen concentration using the constructed laser microfluidic sensor

Microfludic chip irradiated by Diode lasers (532nm) at 100 mW by programming the double syringe pump using Grbl software.

Th value of the incident beam on the solution was obtained inside an acrylic (PMMA) microfluidic channel, and the result was displayed by (Uno laser power meter mW). The intensity is inversely proportion with the increasing in concentration.

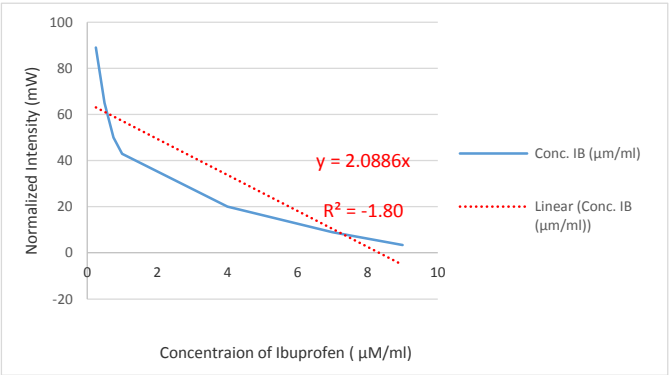


Fig. 5: Calibration curve of Ibuprofen as estimated from laser microfluidic sensor

Then these results were compared with the results from UV-VIS. Figure (6) represented the calibration curve of Ibuprofen that extracted from UV-VIS spectrophotometer.

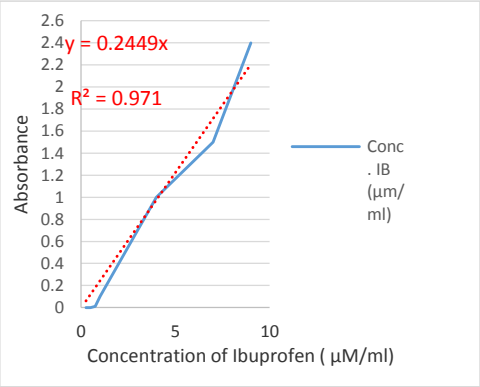


Fig. 6: calibration curve of Ibuprofen from UV-VIS spectrum

From figures 5& 6 the precision, recovery, linearity, and LOD can be extracted as listed in table 1

Table (1): Parameters of the two analytical methods to determine IB concentration

parameters	**Laser microfluidic sensor**	**Uv-vis**
Correlation coefficient (R^2)	**1.801**	**0.97**
LOD (μg/mL)	**0.25**	**1**
Recovery	**99.7**	**98.5**
linearity	**0.25-9**	**1-9**

4. Conclusion

As a new platform, microfluidic instruments offer a lot of potential. More than 20 years ago, microfluidic technologies started to make a difference in biological research. Microfluidic devices have a lot of potential. Studies have shown that it is a developing Microfluidics technology. Owing to their high throughput, great sensitivity, and low cost, is invaluable for research, cost, reduced material usage, and enhanced spatiotemporal control. Additionally, portable microfluidic equipment is available.

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بناء جهاز موائع جزيئي متكامل حساس ومنخفض التكلفة وسريع مع مضخة حقن

لتحليل الإيبوبروفين

هدى ساكن عزت رواء احمد فارس
جامعة بغداد/ معهد الليزر للدراسات العليا

الخلاصة: تقدم أجهزة ميكروفلويديك مزايا فريدة لتطوير مقايسة وفحص الأدوية بكفاءة. قد توفر منصات ميكروفلويديك بديلًا أكثر سرعة وفعالية من حيث التكلفة. تنحصر السوائل في الأجهزة التي لها أبعاد كبيرة على مقياس ميكرومتر. بسبب هذه الابعاد الصغيرة ، فإن الأحجام المستخدمة في فحوصات الأدوية صغيرة (مليلتر إلى فيمتولتر).

في هذا البحث ، تتكون شريحة ميكروفلويديك من قنوات ميكروية منحوتة على مواد ركيزة مبنية باستخدام شريحة أكريليك (بولي ميثيل ميثاكريلات ، PMMA) تم تصميمها باستخدام آلة ليزر ثاني أكسيد الكربون (CO_2). تؤثر معلمات ثاني أكسيد الكربون على عرض وعمق وخشونة الرقاقة. من أجل الحصول على سطح قناة منتظم ، وخشونة منخفضة ، قوة الليزر (60 واط) ، مع سرعة مسح (250 م / ث) للسماح لنا بالحصول على قنوات صغيرة بقطر أدنى من العرض (450 ميكرومتر) ، وكان عمق القنوات 89.4 ميكرومتر و (متوسط الخشونة الحسابي Ra = 2.3) ، (الخشونة النسبية ، ε = 5٪) للسطح بدقة عالية وجودة سطح جيدة.

تم استخدام الأنابيب النانوية الكربونية متعددة الجدران الوظيفية (F-MWCNTs) لتعزيز إشارة الدواء من أجل اكتشاف تركيز الإيبوبروفين القليل جدًا. في هذا العمل ، يتمتع مستشعر الموائع الدقيقة بالليزر بدقة عالية في الكشف عن الإيبوبروفين مقارنة بمقياس الطيف الضوئي بالطريقة التقليدية (UV-VIS) مع LOD يساوي 250 نانومتر ، 1 ميكرومتر على التوالي.