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Optical Fiber Biosensor for Thyroid Gland Hormon Levels Detection

A Thesis

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By

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

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Dedication

This work is dedicated to my parents and My sisters and the reason for my success, the shine of my life, who gives me support and force in every step of the road I would also like to dedicate this work to my friends and the community of support to which I am eternally indebted. Lastly to the men, women, boys, girls, and who came before me, who stand with me, and those who shall come after me who have chosen to live their lives courageously, simply, and "out" on their own terms. It is by the inspiration that this work came to fruition.

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Abstract

Hormones are chemical transmitters that have specific regulatory effects on organs or specific cells. They are responsible for regulating growth, metabolism, reproduction, and other reactions. Three types of hormones are used in this work which are thyroid hormones (Thyroid-stimulating hormone (TSH) and thyroxin (T4) and Triiodothyronine (T3)). Where they are measured by the ordinary method such as on Vida's family instruments to quantitative measurement of total thyroid hormones in, human serum (lithium heparin) using ELFA (Enzyme-Linked Fluorescent Assay) and others which were expensive and required time and efforts. So we decide to use a new method for the detection of these hormones optically by using an optical biosensor which is more accurate, less time, less cost, and effort. The optical biosensor is a device that uses an optical field to detect and measure different biological species such as DNA, cells, and proteins, and any biological specimens with more accuracy. The aim of the present study is detection the level of thyroid hormones (Thyroid-stimulating hormone (TSH), thyroxin (T4), and Triiodothyronine (T3) hormone) and their concentration through the use of two setups of laser biosensors as a new method. At a Specialist Center for Endocrinology and Diabetes (SCED), Forty-five blood samples were taken from patients, between (20 and 50) years old where 15 serum blood samples were collected for each hormone of the thyroid (T3, T4, and TSH) and 5 serum blood samples from normal for each hormone as a control. TSH samples collected from patients composed of (2 males and 13 females) and from healthy people (4 females, 1 male), T4 hormone was collected from (3 males and 12 female) and from healthy people as a (3 females, 2 males), and T3 hormone sample from the patient (4 males and 11 females), while the control was collected from healthy people (4 females, 1 male). In this

work tow setup of the optical biosensors is used to disclose the concentricity of thyroid hormone (Single-mode fiber optical sensor (SMF1, SMF2) and Multimode fiber optical sensor (MMF1, MMF2). The results of absorption of laser light by highly concentrated samples are higher and inversely proportional to the intensity of light, this means that the intensity of light at the detector side was high when the concentration of hormones was low. The mean $\pm$ SD of the intensity of serum T4 between SMF1, SMF2, MMF1 and MMF2 were significantly ($p \leq 0.05$). However, the mean $\pm$ SD of the intensity of serum TSH between SMF1, SMF2, MMF1, and MMF2 were significant ($p \leq 0.01$). While the mean + SD values of the measured serum T3 between SMF1, SMF2, MMF1, and MMF2 were Non-Significant ($P=0.210$). This phenomenon could be explained as, the higher absorption of light by samples (TSH, T4, and T3 hormone) due to the selection of suitable laser which depends on the absorption of the samples to the wavelength of the laser. Multimode fiber optical biosensor of one sensor (MMF1) biosensor considered the more effective type because the signal of the intensity of multimode fiber has a large number of modes compared with single-mode fiber (SMF1, SMF2) and multimode fiber (MMF2). In the construction of two setup types biosensor (single-mode, multimode (SMF1, SMF2, MMF1 and MMF2) using a blue light diode laser (450nm) to measure the level of (TSH, T4 and T3) in blood samples, multimode laser biosensor considered the best biosensor for detection the concentration of three hormones in the sample in addition it is highly sensitive in the transmission of signal light intensity. A biosensor is the most accurate, with a rapid diagnosis, less costly method than the traditional method to avoid any biological changes in blood sample lead to changes in optical characteristics (absorption) of the blood sample.

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List of abbreviations

Abbreviations	Meaning
ACTH	Adrenocorticotrophic hormone
Na	Cladding index
E	Energy
FSH	Follicle-stimulating hormone
GH	Growth hormone
LSD	Least significant difference
LASER	Light amplification by stimulated emission of radiation
LH	Luteinizing hormone
M	Micrometers
MMF	Multimode fiber
Nm	Nano meter
H	Planks constant
N	Pulp refractive coefficient
PCF	Photonic crystal fiber
SMF	Single-mode fibers
SCED	Specialist center for endocrinology and diabetes
SCH	Subclinical hypothyroidism
V	The speed of light in matter
C	The speed of light in vacuum
TPO	Thyroid enzyme peroxidase
TH	Thyroid hormone
TSH	Thyroid stimulating hormone
TSHR	Thyroid stimulating hormone receptor
TRH	Thyrotropin releasing hormone
T4	Thyroxine
TBG	Thyroxine binding globulin
T3	Triiodothyronine
λ	Wavelength



Chapter one

Introduction and Basic concepts

1. Introduction

This chapter focusing on the hormones secreted from the endocrine glands such as Thyroid stimulated hormone (TSH) produced from the pituitary gland, triiodothyronine (T3) and thyroxine (T4) which are produced from the thyroid gland. Then define Laser, biosensor, optical fibers and evanescent wave.

- **Aim of study**
- The first part focuses on, equipment and materials that had been used to collect biological samples (blood) from patients of the hyperthyroidism and hypothyroidism and measuring concentrations of thyroid hormones (T3, T4, and TSH) manually in the specialist center for endocrinology and diabetes using the Vida's kit.
- The second part focuses on the method of biosensors designing with two setups. The first one is single and multimode optical biosensor of one sense (SMF1 and MMF1) while the other set up is single and multimode the optical biosensor of two senses (SMF2 and MMF2).
- The third part focused on the method of detection of the thyroid hormones (T3&T4 and TSH) and its concentration spectrally.

1.1 The Endocrine System

A control system of ductless glands that excrete hormones inside particular organs is called the endocrine system where the Hormones act as "messengers," and transfer by the bloodstream to various cells in the body. [1]

1.1.1 The pituitary gland

The pituitary is an organ of major importance in the endocrine system. The adenohypophysis portion of the pituitary produces several hormones [2]. Hypothalamic –pituitary – thyroid axis as shown in figure (1-1) regulates the production of thyroid hormones where the thyroid-stimulated hormones TSH could stimulate the secretion of thyroid hormones in response to thyroid releasing hormones (TRH) which is produced by the hypothalamus. TRH transported to the pituitary gland through the hypothalamic hypophyseal portal system. So by the negative feedback of T3 and T4, the TSH and TRH were regulated. Other hormones such as glucocorticoids, somatostatin, dopamine, prolactin, estrogen, and growth hormones could influence the levels of the thyroid hormones [3]. As shown in figure (1-1).

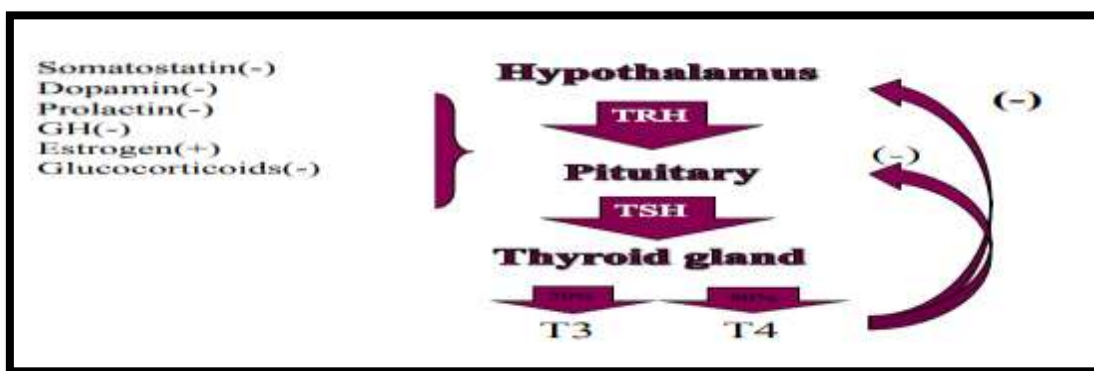


Figure (1-1) the hypothalamic-pituitary-thyroid axis.

A series of differentiation events and the proliferation of regulated cellular give rise to five highly differentiated cell kinds secreted six hormones:

- Adrenocorticotrophic hormone (ACTH) from the corticotrophs.
- Thyrotropin or thyroid-stimulating hormone (TSH) from the thyrotrophin,

- Growth hormone (GH) from the somatotrophs,
- Prolactin from the lactotrophs.
- Follicle-stimulating hormone (FSH).
- Luteinizing hormone (LH) from the gonadotrophs [4].

1.1.2 Thyroid gland

The thyroid gland is a section of the body's endocrine device. It is a great organ specializing in an endocrine job in the human body. It is a butterfly-shaped gland as shown in figure (1-2) with many veins, anchored around the front of the throat near the voice box [5].

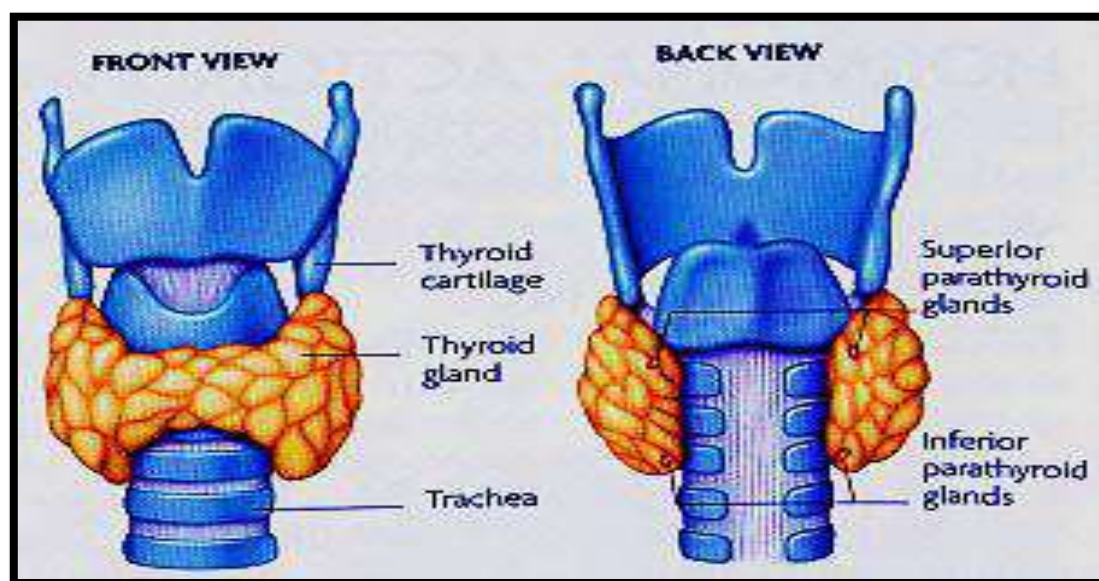


Figure (1-2) the thyroid gland [6]

The gland is made up of thousands of follicles, every which is a spherical cyst of epithelial cells (thyrocytes) surrounding the cavity that contains a colloidal, reservoir of thyroid hormone precursors, Globulin. The average follicle diameter is 300 microns. The epithelium of the normal gland usually described as a cube, with a top plasma membrane (facing the follicle cavity) and the basal plasma membrane in the opposite position. The most obvious structural difference between the top cell surface and the

lateral surface is that the only former furnished with pseudopods. Differences in enzyme components between the two domains shown via cytochemical Studies such as the presence of peroxides, aminopeptidase, and H_2O_2 generating activity only on the top surface and Na /K ATPase only on the underside Surface - exterior appearance. The thyroid gland secretes three hormones: thyroxine hormone (T4) and triiodothyronine (T3) where they are iodinated derivatives of tyrosine and calcitonin, a polypeptide hormone and produced by follicular cells while calcitonin is secreted by cells (C) which called perifollicular cells. These cells are separate from the embryonic origin. Calcitonin is not functionally related to the other thyroid hormones. It has a secondary role in calcium stability [7]. The thyroid hormone is created by the thyroid gland, which is found in the abdomen of the thyroid cartilage. From a metathesis, the thyroid gland consists mainly of spherical follicles. Each follicle consists of a colloidal cavity surrounded by epithelial cells or thyroid cells. A smaller group of different cells, C cells, are distributed between follicles and are involved in Ca^{2+} -homeostasis. Thyroid hormone synthesis is a multi-step process that occurs in the follicles. [23]

1.1.2.1 Physiology of thyroid gland

The essential function of the thyroid gland was the production of hormones. Thyroxine (T4), triiodothyronine (T3), and calcitonin. Up to (80%) of (T4) is changed to (T3) by peripheral members such as the spleen, liver & kidneys. The activity of T3 is (10 times) more than T4. follicular cells synthesis Thyroxine (T4) from free tyrosine and on the residue of the protein named thyroglobulin (TG). Iodine was captured together with the "iodine trap" via hydrogen peroxide produced by the thyroid enzyme

Peroxidase (TPO) [8]. Then attached to sites 3' and 5' of the benzene ring tyrosine residues on TG and free tyrosine. The follicular cells reabsorb TG and T₃, one absent like compared to T₄), and releases it into the blood. Deiodinase enzymes transform T₄ to T₃ when stimulated by thyroid-stimulating hormone (TSH). About 90% of thyroid hormone that excreted is T₄ and 10% is T₃ [9]. In the blood, T₄ and T₃ are partly associated with globulin associated with thyroid hormone, albumin and transthyretin [10]. The figure (1-3) shows thyroid gland and anatomic relationships [11].

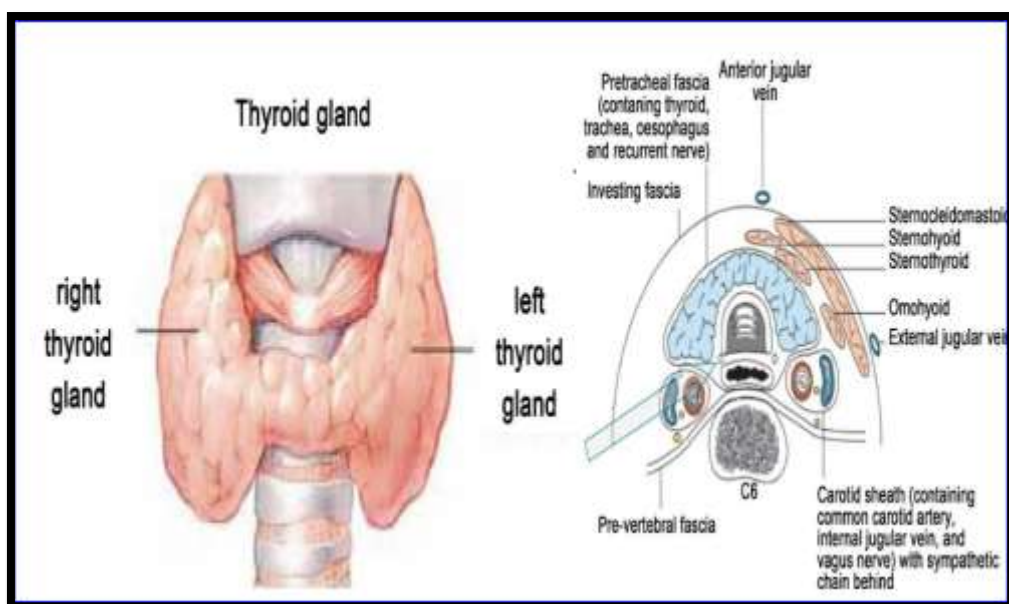


Figure (1-3) anatomic relationships of the thyroid gland [11]

1.1.2.2 The major functions of the thyroid gland

- It has a turn in Development. [12].
- It has a turn in the growth [13].
- It catalyzes the heart rate [14].
- It catalyzes heart contraction [15].
- Stimulate synthesis of proteins [16].
- Stimulate the synthesis of carbohydrates [17].
- Decomposition cholesterol and triglycerides [18].

-
- Increases vitamin requirements [19].
 - Promote the beta-adrenergic receptor for catechol amines [20].

1.2 Thyroid hormone (TH)

Thyroid hormone regulates metabolic processes necessary for normal outgrowth and evolution in addition to regulating metabolism in adults. It is established that the condition of the thyroid hormone is related to body weight and energy disbursement. Hyperthyroidism, promotes excessive metabolic status characterized by increased energy consumption during rest, weight loss, low cholesterol levels, increased fat decomposition, and glucose formation. On the contrary, hypothyroidism, low levels of thyroid hormone, is associated with a lack of metabolism which is characterized by low resting energy consumption, weight gain, increased cholesterol levels, low-fat degradation, and reduced sugar development. TH catalyzes both lip formation and fat decomposition, although TH levels are high, the net effect is fat loss [21]. figure (1-4) shows production and action of thyroid hormone.

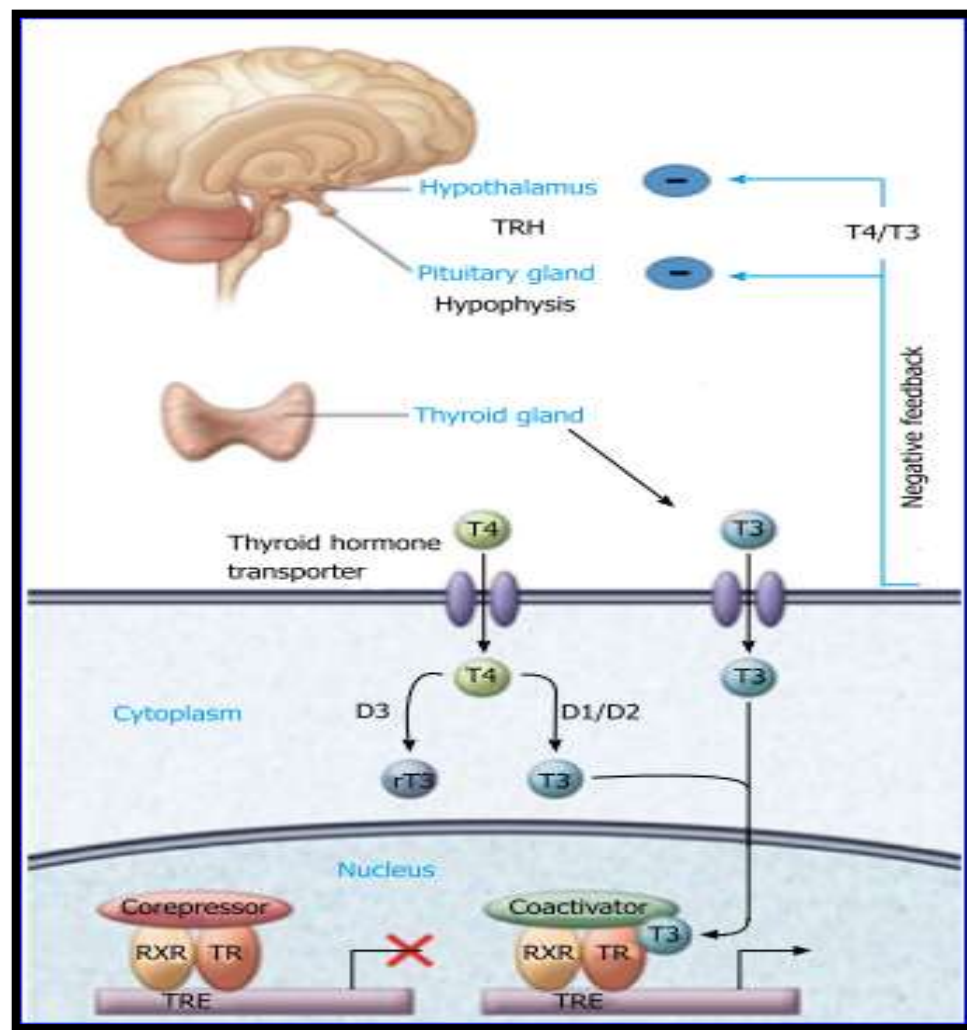


Figure (1-4) production and action of thyroid hormone [22]

1.2.1 Types of thyroid hormone

1.2.1.1 Thyroid-stimulating hormones (TSH)

Thyroid-stimulating hormone (TSH, thyrotropin) and TSH receptor (TSHR) are key proteins in the control of thyroid function. TSH synthesis in the anterior pituitary is stimulated by thyrotropin-releasing hormone (TRH) and inhibited by thyroid hormone in a classical endocrine negative-feedback loop. TSH controls thyroid function upon its interaction with the G protein-coupled (TSHR) [24]. TSH stimulates most, if not all, biosynthesis steps of thyroid hormones, from iodine absorption (by

enhancing NIS expression) to tag absorption of run-up cavity and the resulting secretion of thyroid hormones in the bloodstream. TSH secretion is stimulated by TRH, which is produced in turn by neurons in the nucleus Ventricular in the hypothalamus area, prevents hypothyroidism [25]. TSH associated with and its receptor on thyroid cells leads to Stimulating the prophet's second paths Mostly camp, in high concentrations, inositol triphosphate (IP3), and Ed Islet Glycerol (DAG), which eventually led to the modification of the gene expression of the thyroid gland .Physiological roles of TSH include stimulation of differentiated thyroid functions, such as iodine uptake and organification, production and release of iodothyronines from the gland, and promotion of thyroid growth. TSH also acts as a factor protecting thyroid cells from apoptosis and plays a critical role in ontogeny. In a mouse model with targeted disruption of the common α -subunit gene and thus devoid circulating glycoprotein hormones, thyroid development was arrested in late gestation [26].

1.2.1.2 Thyroid Hormone Triiodothyronine (T3)

Triiodothyronine is the thyroid hormone that have plenty important roles in the metabolism and heart rate, functions in digestion, muscle control, function and development of brain, and bone maintenance [27]. Most of the T4 is converted into T3 by removing the iodine from the thyronine ring by special enzymes (deiodinase) type1, 2, and 3 each one has its own target, after deiodination T3 is formed and can do it metabolic activities [28]. T3 forms twenty percent of the thyroid hormones productions and the rest of it comes from T4 deiodination, the powerful of action of T3 is four times more than T4 [32].

1.2.1.3 The Thyroid hormones thyroxin (T4)

Thyroid hormone is a unit of the thyroid hormones that account for 80 percent of Thyroid output, also called thyroxine, which is called tetra iodothyronine because it contains four iodine atoms to do its work, it is converted into tri-iodothyronine when travels to the organs such as the kidney, liver and others to do its action it's converted into triiodothyronine because it's the active form of the hormone [29] [30]. The half-life of the T4 hormone is (6 Days) in the serum, it is relatively long. Thyroxine linked tightly binding to the protein of serum globin (TBG), albumin, and transthyretin. The importance of these proteins is the transport of thyroid hormones to their place of action because of its water-hater properties that enable it to attach to any available surface and quickly escape from the aquatic environment [31]. A prohormone, T4 is a reservoir hormone for an active thyroid hormone T3, which is four times more effective. In tissues, T4 is converted by deiodinases to T3 [21]. The importance of L-thyroxin, the main hormone produced by the thyroid gland, biologically is well established, but the mechanization of thyroid hormone work remains largely unjustified. L-thyroxin has crystallized and identified its three-dimensional structure by X-ray crystals in the hope that comparing the structures of active and inactive thyroid hormone isotopes will shed some light on the mechanisms of hormones [33].

1.2.2 Thyroid Dysfunction

Dysfunction of the thyroid gland, pituitary gland, or hypothalamus result in an imbalance of thyroid hormone productions. The pituitary, which is control T3, produces TSH and T4 production and TRH synthesized by the hypothalamus and control the TSH production [34]. Disorder in thyroid hormone may come from iodine which is a key

determinant for thyroid disease risk, aging, smoking, genetic susceptibility, ethnicity, and any endocrine disorder also therapeutics, including immune checkpoint inhibitors are influenced disease in the thyroid [35].

1.2.2.1 Subclinical hypothyroidism (SCH)

Defined as a high level of thyroid hormone (TSH) in the blood with normal free thyroid hormone values. Subclinical hypothyroidism is spread from (3 to 8) percent in the general population, and up to (15 to 18) percent in women older than (60) years of age [36].

1.2.2.2 Subclinical hyperthyroidism

Subclinical hyperthyroidism is known by lower or undetectable thyroid activating hormone levels, with free natural thyroid hormone levels and total or free triiodothyronine levels. It can be caused by increased internal production of thyroid hormone (such as in Graves' disease or toxic nodule thyroid hypertrophy), or the administration of thyroid hormone for the therapy of malignant thyroid illnesses, or unintentional too much treatment of thyroid hormone. [37]

1.2.2.3 Hypothyroidism

Hypothyroidism is a disorder that occurs when the thyroid gland does not produce sufficient thyroid hormone to meet the needs of the body. The thyroid hormone organizes metabolism (the way the body uses energy) and nearly every organ in the body. Without enough thyroid hormone, many of the body's functions slow down [38]. The decrease in thyroid hormone production and thyroid gland function represent hypothyroidism caused by acute and chronic iron deficiency Thyroiditis (Hashimoto's disease) and lack of motivation, Radioactive iodine that causes follicles

destruction, surgery and pharmacological agents like lithium and amiodarone, the last. It's an anti-arrhythmia. This condition can be classified into two categories: Basic hypothyroidism, which the disadvantage is the thyroid gland or secondary hypothyroidism, where it can cause other diseases Indirect decrease in the circulatory hormone, for example, a surgical or pathological change. [39]

1.2.2.4 Hyperthyroidism

Hyperthyroidism refers to any condition in which too much thyroid hormone is produced in the body. In other words, the thyroid gland is hyperactive. Another expression you may hear of this problem is thyroid poisoning, which refers to high levels of thyroid hormone in the bloodstream, regardless of its source [40]. Heart symptoms of hyperthyroidism may appear in the form of as an outcome of both hyperthyroidism and its effect on already existed heart illnesses [41]. The thyroid affects the cardio-vascular system on various Ways. It has a direct effect through the positive and non-positive chronographic effect in addition to interfering with peripheral resistance and blood cardiovascular effect is amplified or more pronounced Increase of ren epinephrine receptors within the heart are also important thyroid hormonal action as well. All cardiovascular events are related hyperthyroidism is called an overly dynamic circulation condition. It usually occurs as an automatic increase in cardiac output and increases. In systolic pressure due to reduced resistance to peripheral blood vessels diastolic hypotension. Short-lived concentration [42]. It is hit about 2.0% of women and 0.2% of men worldwide [43].

1.3 Laser

LASER (Light Amplification by Stimulated Emission of Radiation)

LASER is an abbreviation for amplifying light by emitting stimulated radiation. Although considered as one of the non-conventional processes, laser material processing (LMP) is no longer in its infancy [44]. The laser delivers coherent, monochromatic, well-controlled, and precisely directed light beams [45]. Einstein introduced the first theoretical basis of LASER and MASER in 1917 using the Planck Radiation Act, which relied on probability coefficients (Einstein coefficients) for the absorption and spontaneous emission of electromagnetic radiation. Theodore Mailman was the initial who shows practical lasers in 1960 after many scientists reported, including the premier theoretic description of RW [46]. The laser is simply an oscillator of light, and the phenomenon of oscillation is one of its underlying foundational principles [47]. As shown in figure (1-5)

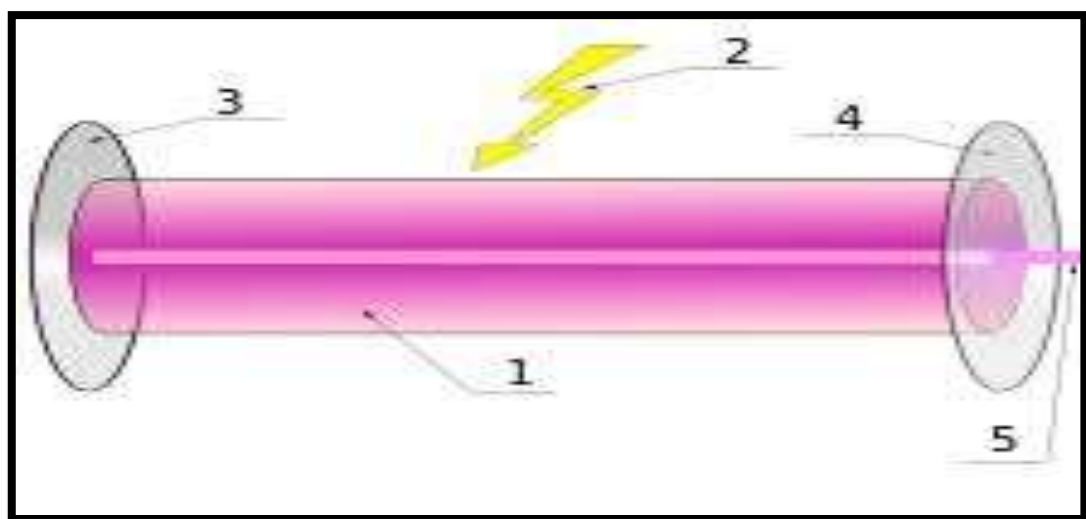


Figure (1-5) Components of a typical laser

1. Gain medium
2. Laser pumping energy
3. High reflector
4. Output coupler.
5. Laser beam [48].

1.3.1 Components of the Laser system

The main component of the laser is so simple. It contains a Laser medium placed inside the optical cavity, pump power exporter, and cooling system. To contain and amplify the serial photon on reaction, it is needful to place that reaction inside the wide optical cavity. The optical cavity consists of two parallel mirrors placed on each side of the center of the lasing or laser medium. Mirrors are discrete a constant distance (D), to form a Fabry -Perot interferometer. Lasing Medium could be the solid state, gas, liquid-dye, semiconductor-diode, or indecent electron lasers-FELs - Pump exporter. In this configuration, photons bounce off mirrors and return to the center to stimulate the release of more photons. Mirrors unite light. That is, photons that are completely perpendicular to mirrors enter the active medium, while the photons at the axis leave the laser process. Because the process is not 100% effective and some energy is converted to heat, a cooling system is provided. If one mirror is completely reflective (M_2), the other mirror (M_1) is partially conveyed, the other mirror (M_1) is partially conveyed. The light that leaks through the M_1 becomes a laser beam. the laser is named after the contents of the active medium and the status of its suspension. [49]. As shown in figure [1-6]

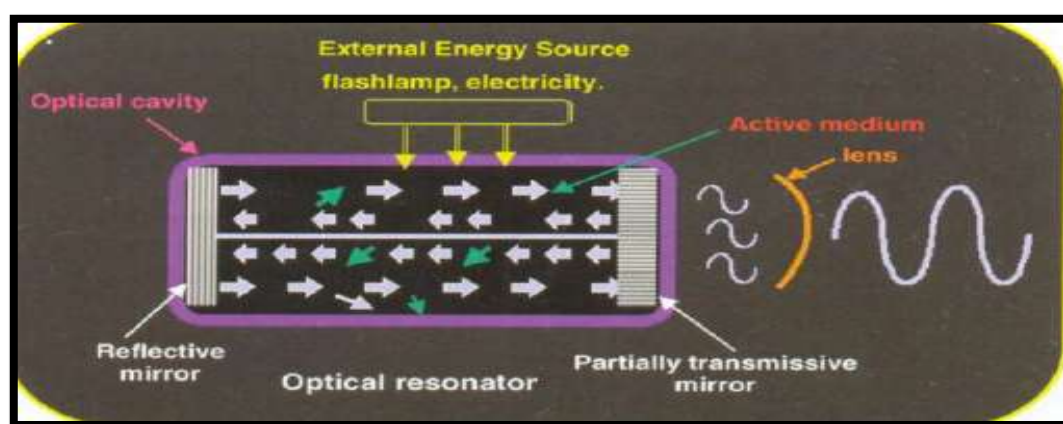


Figure (1-6) Components of the Laser system [49]

1.3.2 Kinds of lasers

According to the active medium types, the laser can be classifying as:

- Liquid Laser.
- Gas Laser.
- Solid Laser. [50].

1.3.3 Operation of laser

1.3.3.1 How lasers emit light

The essential components of the laser are the active medium and resonator where they control the process of stimulation and emission of laser light. [51]

1.3.3.2 Absorption

The absorption of electromagnetic radiation is the route in which the energy of the photon is absorbed by the material, usually the electron of the atom. Consequently, electromagnetic energy is converted to other forms of energy for, example, temperature. When the photon absorbs energy, $h\nu = E_2 - E_1$, the atom jumps from level 1 to level 2. The operation occurs with a realistic photon as shown in Figure [51] Absorption in addition to dispersion effects that limit light transmission through a full range of fallen light, the potential transmission window of the glass is limited by absorption [52] as shown in figure (1-7).

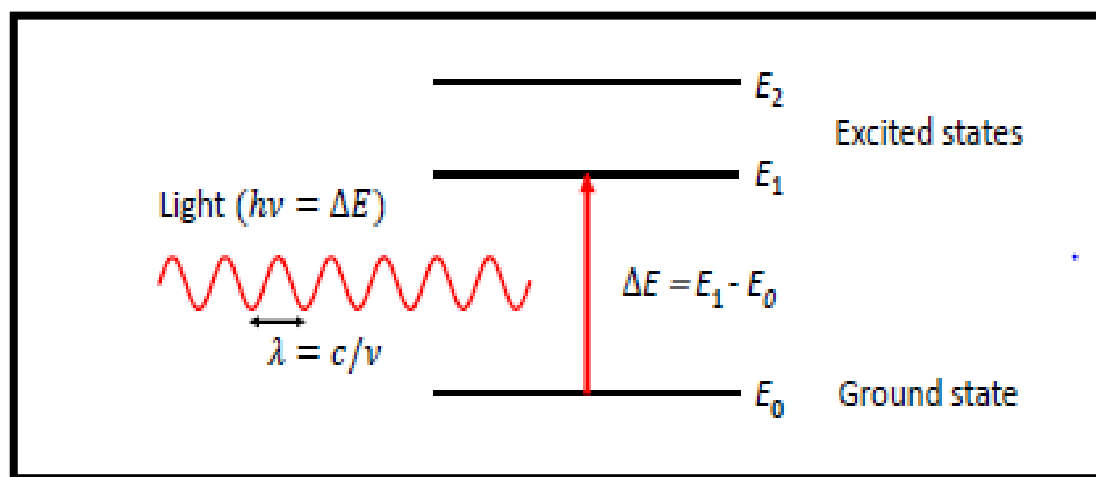


Figure (1-7) Absorption [53]

Ground state (lowest possible power) at E_0 power can be moved to a higher level when energy E_n if the molecule is absorbed Electromagnetic radiation of the corresponding wavelength $\lambda = c/\nu$, $h\nu = (E_1 - E_0)$, where c The speed of light and h is constant Planck. There are usually only exciting cases of a very short period of time (mint to seconds to microseconds), because the state of higher energy unstable and loses extra energy through relaxation processes such as emission Light [53].

1.3.3 3. Stimulated emission and Spontaneous emission

Stimulated emission is a process, where the incident electromagnetic field including single-photon energy, forces an atom in its excited state (terrestrial) to oscillate and produce a second electromagnetic field, containing one photon energy, which is in phase (anti-phase) with the field of the accident so that these two opposing fields are with the incident so that these two fields overlap constructively (destructively) with each other and emit energy (absorbing) each other from each other atom. Spontaneous emission is a process in which the atom in its raised state produces an electromagnetic field, which collects single photon energy,

with a random stage in relation to a present accident field [54]. As shown in figure (1-8).

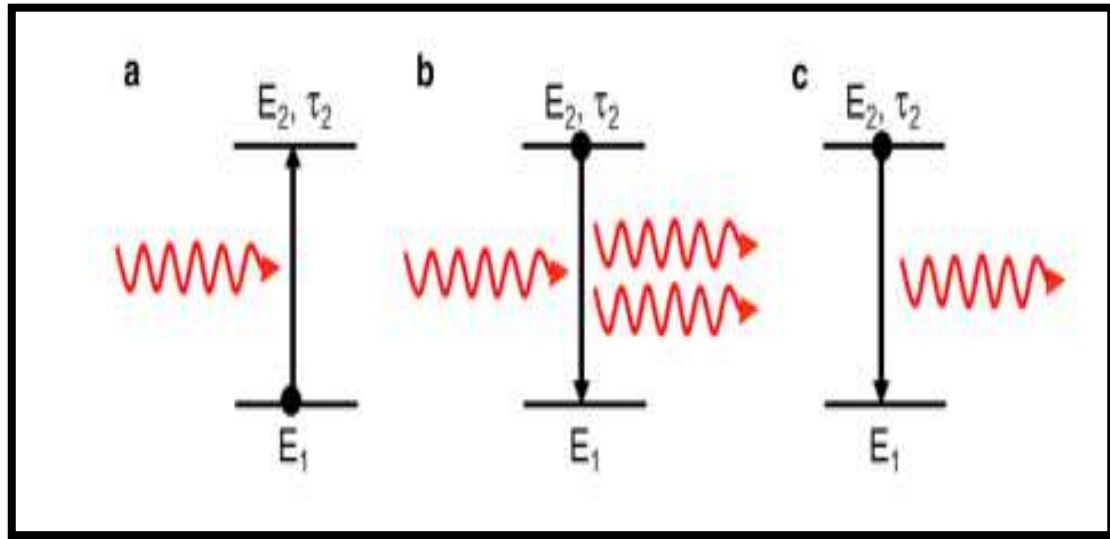


Figure (1-8) The processes of (a) absorption, (b) stimulated emission, and (c) spontaneous emission by a two-level atom with level energies E_1 and E_2 . [54]

1.3.3.4 Population inversion

The catalytic emission effectively doubles the light. By cyclic this individual phenomenon several times, it is possible to generate a light in which all photons are identical. Each photon is a replica of others, the same color, the same moment of emission, and the same direction of motion. This is laser light. The discovery of induced emission was not, in itself, sufficient to develop a laser. In normal matter, more atoms, ions, or molecules are in an unexcited state than in an excited. In this case, it can't generate enough catalytic emission to produce a light laser. What we need is a way to change the state of the medium so that there are more exciting

particles (ions, atoms, or molecules) than there are particles at rest. This operation is called population inversion [55].

1.3.3.5 Lasing Threshold

It is the lowest level of excitement in which laser output is stimulated rather than spontaneously emitted. Below the threshold, the energy of the laser output rises slowly as the excitement increases. Above the threshold, the inclination of force versus excitement is much greater. The width of the laser emission line also becomes smaller than the threshold. Above the threshold, the laser said to be laser-operated. All these processes occur in a laser gain medium. Lasers are often classical depending on the nature of the pumping process, which is the energy source of the resulting laser beam. In laser electrical discharge, for example, Pumping occurs as a result of an election collision in gas discharge with the atoms of the gain medium. [51]

1.3.4 Laser hazard and safety

- Avoid looking directly into any laser beam or at its reflection.
- Remove all unnecessary specular (shiny) reflecting surfaces from the work area.
- Operate lasers in well-defined areas to which access can be controlled. The area should be posted with appropriate signs to alert persons passing by the area that a potential hazard exists.
- The laser system should be operated only by or under the direct supervision of a person knowledgeable of the hazards and control methods for both beam and non-beam conditions. This individual is usually the laser safety officer (LSO) who is designated by the

administration of the company, hospital, or educational institution. The LSO shall have the authority and the responsibility to effect monitoring and enforce the control of laser hazards and to achieve the knowledgeable control of laser hazards.

- Any accident should immediately be reported to the responsible medical authority. If there is an accidental exposure to the eye, the services of an ophthalmologist should be sought. [56]

1.4 Biosensor

A biosensor is a pooling tool, in close contact, an identification element with a conversion device. The common of all these tools is the support material, on one of the converging partners (the recognition element) installed. It could be partners. Enzyme and its substrates, a pair of antibodies/antigen, receptors and their specific bond, or even living cells and analytical material specifically related to it. To detect the interaction of this pair, the biosensor uses a sensor, or an adapter converts the biological response to the electrical signal is amplified, stored and quantify by the processor. [57]

1.4.1 The basic characteristics of the biosensor

- Linearity- The linearity of the sensor must be high to detect high substrate concentrations.
- Sensitivity -The value of electrode response for each substrate concentrations.
- Selectivity- Chemical interference should be minimized to get the correct result.
- Response Time- The time needed to get 95% of the response. [58]

1.4.2 The disadvantage of biosensors

- Temperature parameter affects biosensor sensitivity performance.
- pH parameter influences the performance.
- Sample preparation requirements.
- Tedious measurement conditions [59].

1.4.3 Kind of Biosensors

- Resonant Biosensor.
- Optical biosensors.
- Thermal Biosensors.
- Electrochemical Biosensors.
- Bioluminescence sensors.
- Nucleic Acid-based Biosensors.
- Nano biosensors [60].

1.5 Optical biosensors

Optical biosensors present great characteristics compared to traditional analytical techniques because they allow direct, realistic, and label-free detection of many biological and chemical materials. Its features include high privacy, sensitivity, little size, and cost-effectiveness [61]. Biochemical processes play a very important role in medicine, biology, and biotechnology. However, it is very rough to convert biological data directly into an electrical signal, biosensors can transform these signals and biological sensors to this difficulty. In recent years, thanks to improved technologies and devices, the use of these products has increased [62]. While sensors have himself group of components light sources and optical

fiber to direct light between them and the optical detectors. So Understanding the principle of the action of different fiber optic sensors, it is important to find out the optical components used [63]. As shown in figure (1-9).

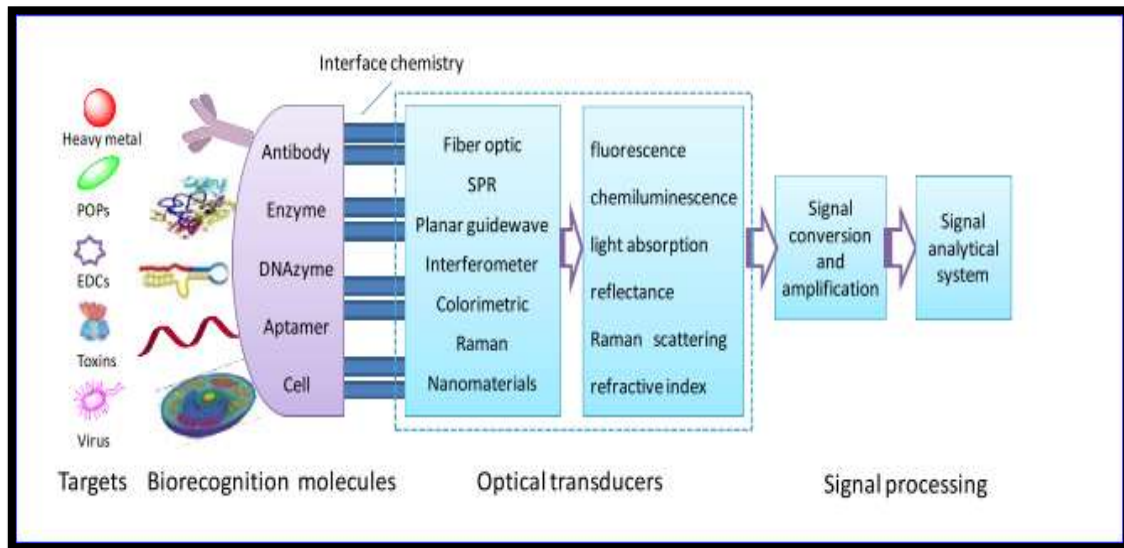


Figure (1-9) Schematic of an optical biosensor [64]

1.5.1 Fiber-optic biosensors of absorption

That kind of biosensor mensuration the transmitted light scattered via the fiber and then mensuration absorption amount using the Lambert Bear Act as described in equation (1).

Lambert Bear's Law used to absorb.

$$A = \log \left(\frac{I_0}{I} \right) = \epsilon \cdot [C] \cdot l$$

Where is

A = visual absorption.

I_0 = intensity of accident light.

I = the intensity of the light transmitted.

ϵ = mole absorption factor. [65]

1.5.2 Fluorescence Fiber-Optic Biosensors

The use of fluorescence fiber-optic biosensors leads to the detection of signals by transferring the excitation light through an optical fiber; the emitted light is then measured via a detector. The change in fluorescence intensity is related to the analyte concentration. Fluorescence fiber-optic biosensors are a better option when compared to absorption sensors due to their ability to measure low concentrations of analyte. [65]

1.5.3 Optical waveguide based biosensors

In the previous section, we have discussed interferometer based Optical waveguide based biosensors in the previous section, we have discussed interferometer based Waveguide- In the previous section; we discussed the existing interferometer Biosensors, some of which use waveguide structures as a sensor element. [66] The principle of the optical waveguide is that a low refractive substance that acts as a cladding surrounds a visual matter with a higher refraction coefficient [67]. There are two main classifications of waveguide systems - multimode and individual mode. Multi Waveguides are much thicker than the wavelength of the exciting light, which is usually manufactured using glass materials, polymer, or, silica making it relatively inexpensive and easy to use. Industry. The thickness of the waveguide is in order of several microns, allowing for a simple edge the coupling of the excitement light in the waveguide structure. [68]

1.5.4 Classification of optical biosensors

- * Optical fiber biosensors.
- * Optical sensors based on surface Plasmon ring (SPR).
- * Total Internal Reflection Fluorescence (TIRF) Biosensors.
- * Surface-Enhanced Raman Scattering (SERS). [69]

1.6 Fiber optics

The field of applied sciences and engineering for the design and application of optical fiber is known as an optical fiber. Fiber optics usually have a transparent core surrounded by a transparent cladding material with a low refractive index. Light is retained in the heart by the phenomenon of total internal reflection that makes the fibers act as a waveguide. Cladding surrounded by paint, not the visual layer. It consists of various layers of polymer and paints forms Layer protection of silica structure from unwanted environmental effects The insulator is a layer of about 900 micrometers located around a coating that protects the fiber from breakage while working [70]. As shown in figure (1-10).

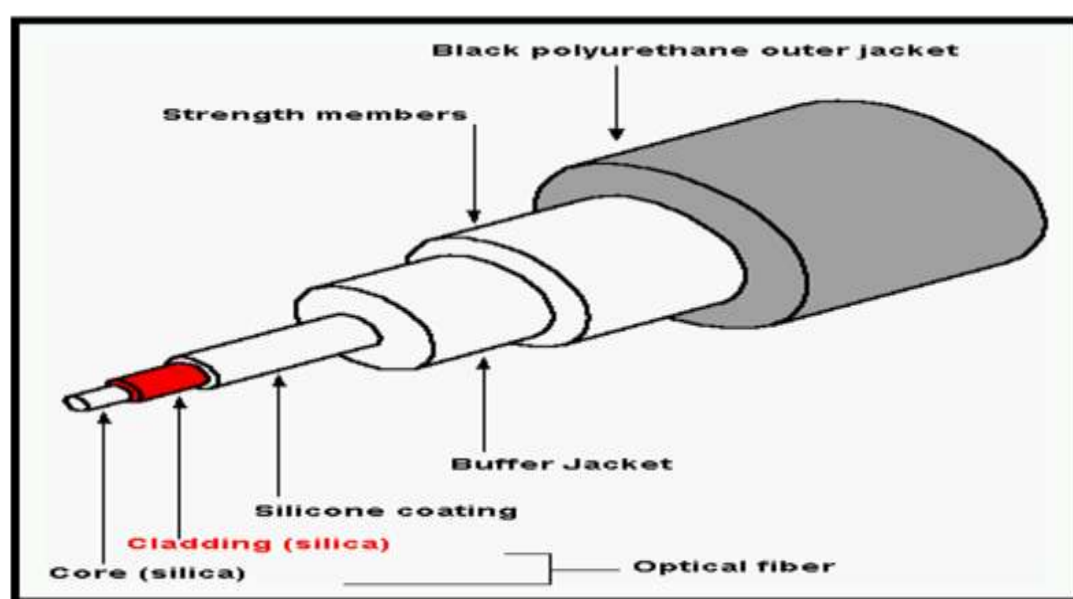


Figure (1-10) Basic structure of an optical fiber [71]

1.6.1 Fiber optics fundamentals

- **Core:** The core is that the central part of the fiber. It is generated from matter things, and the glass usually generates it. Light spreads through the core in the first place.
- **Cladding:** cladding or preventive cover that the outer layer of the nucleus, and, in addition, they were generated from insulating matters. Things with much refractive evidence. The refractive index of cladding or protective the cover is smaller than refractive. Basic Materials Guide. That is probably the part. Made of glass or plastic materials. It reduces the loss of light from the heart to closed air. It's. In addition to reducing the loss of dispersion in the heart surface, protects from fiber interesting surface impurities adds the force of fiber.
- **Insulating or coatings:** exterior paint or jacket Outer layer to protect the fiber from any kind of physical damage. This part of the plastic material. These materials are versatile Circumference to prevent scratches [72].

1.6.2 Fiber optic sensors

Are excellent candidates for monitoring environmental changes and they offer many advantages over conventional electronic sensors as listed below as:

- Easy integration into a wide variety of structures, including composite materials, with little interference due to their small size and cylindrical geometry.
- Inability to conduct electric current.
- Immune to electromagnetic interference and radio frequency interference.
- Lightweight.
- Robust, more resistant to harsh environments.

-
- High sensitivity.
 - Multiplexing capability to form sensing networks.
 - Remote sensing capability.
 - Multifunctional sensing capabilities such as strain, pressure, corrosion, temperature and acoustic signals. [73]

1.6.3 Fiber optic sensor applications

Fiber optic sensors used in many areas specifically [74].

- Monitoring the physical health of facilities in real- time.
- Measuring physical properties: acceleration, pressure, heat, speed, and displacement.
- Measuring the power supply.
- Application to the oil and gas industry, pressure sensor, temperature sensor- Tunnels: multi-point optical expansion gauges, joints that monitor damage detection, and closeness control.
- Heritage structures: post-earthquake damage assessment, old and new interaction, displacement monitoring, restoration monitoring.
- Dams: distributed temperature control, foundation control, spatial displacement measurement, joint expansion. [75] [76].

1.6.4 Operation of Optical Fiber

Turn on the fiber optics on the principle of total internal reflection. The light is reflected (bounces back) or breaks (changes direction during a different medium penetration), depending on the angle at which it hits the surface. Controlling the angle in which light waves are transmitted makes it possible to control how efficiently they reach their destination. Optical waves routed through the heart of the optical fiber in the same way that RF

signals routed over a hub cable. Optical waves are directed to the other end of the fiber through their reflection inside the core the composition of the cladding glass for the heart of the glass determines the ability of fibers to reflect light. This reflection is usually caused by the creation of a higher refractive indicator at the glass top than in round cladding glass, resulting in the creation of a "waveguide". The refractive coefficient of the nucleus is increased by a slight modification of the composition of the base glass, in general by adding small amounts of impurities. Alternatively, the waveguide can be created by reducing the refractive coefficient of cladding using different stimulants. There are two types of fiber optics. [77]

1.6.5 Optical fiber kinds

Optical fiber become labeled into two major kinds [78].

1.6.5.1 Single-Mode Fibers

The core volume of single-mode fiber is little. The size of the core (diameter) is usually about 8 to 10 micrometers (μ m). The core of fiber of that volume is allowed only to place the platform or minimum to spread around the wavelength of 1300 nm (nm). Single-mode fibers are spread in only one mode because the base size approaches the operational wavelength (λ). This is accomplished using lasers as a source of light. [79]. The primary refraction coefficient can be referred to as n , which is larger than the n cladding refraction coefficient. The little diameter of the nucleus lets the transfer of one position of the light. No dispersion, no degeneration of the signal transmitted through the fiber, low attenuation due to the number of waves spreading along with the core of the fiber giving the signal ability to spread over long distances and faster [80]. As shown in figure (1-11)

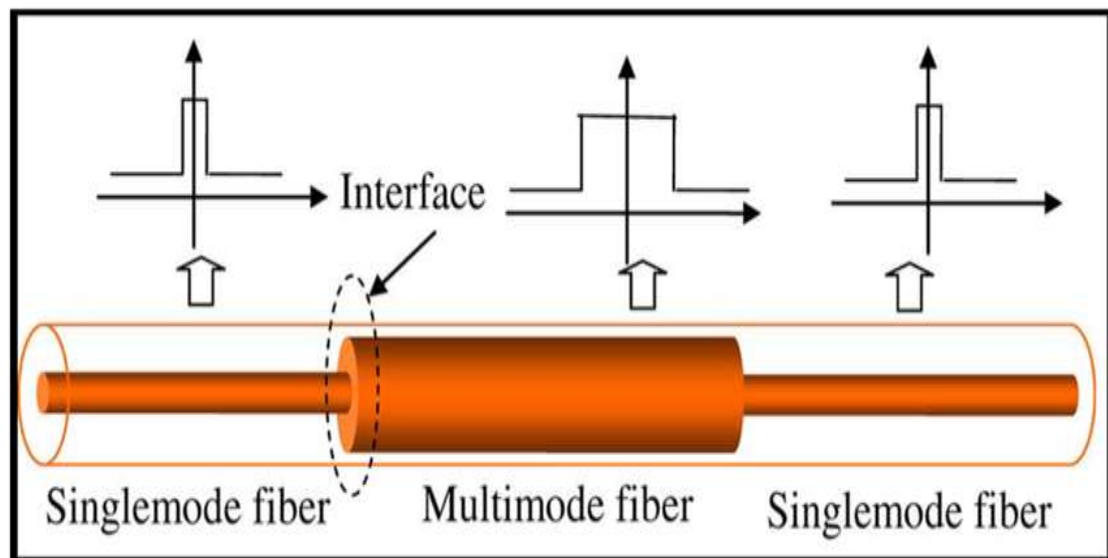


Figure (1-11) Schematic configuration of the single-mode–multimode–single-mode fiber structure. [81]

1.6.5.2 Multimode Fibers

It is a kind of fiber, allowing its structure (the largest diameter of the nucleus) to pass through more than one light radiation with various wavelengths, thus allowing several "modes" of light to enter and exit the fibers. Is based on the reflection on its walls for the spread of light. As shown in figure (1-12)

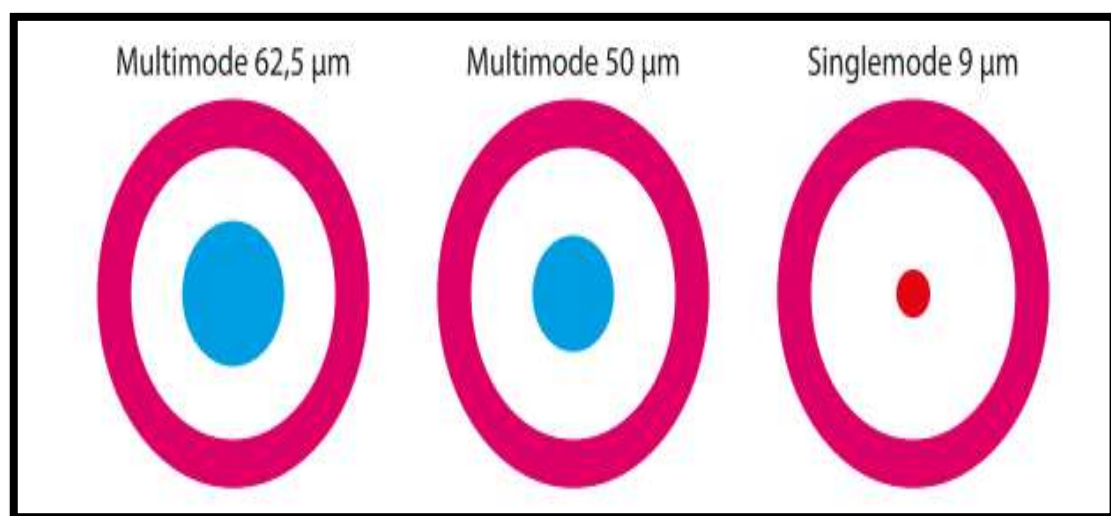


Figure (1-12) Types of optical

The cost of manufacturing single-mode fiber is tall because of the transceiver used. They are laser diodes with more energy and direction than the LED diode that uses multi-position fiber, generating more widespread light [82]. Fiber optic uses three basic types of multi-mode fiber in communication systems (Step-index multimode, Graded-index). [83]

- **Step indicator**

Fiber optics that have a diameter larger than the nucleus (about 50-200 micrometers). In this kind, the path of light spread is zigzag in shape. The pulp refractive coefficient is (n_c) and the cladding index (n_a), the refractive index in the core remains constant (n_c) and suddenly changes to (n_a) inside the cladding. Total internal reflection occurs due to the change in the refractive coefficient in the main cladding façade, where light rays move from the core to the cladding denser to a scarcer medium

- **A Gradient Indicator**

Fiber optics with a hearth diameter of about (50 micrometers). In this type, the path of light is spiral-shaped. The nucleus refractive coefficient (n_c) is at a maximum in the center of the heart and gradually decreases to a minimum value (n_a) in the nucleus cladding interface. Light rays moving below the axis progress slower than those near the cladding because of their differences in refractive indicators. But almost all rays reach the exit at the same time because of the spiral path. Therefore, there is no dispersion [80]. As shown in figure (1-13) and (1-14).

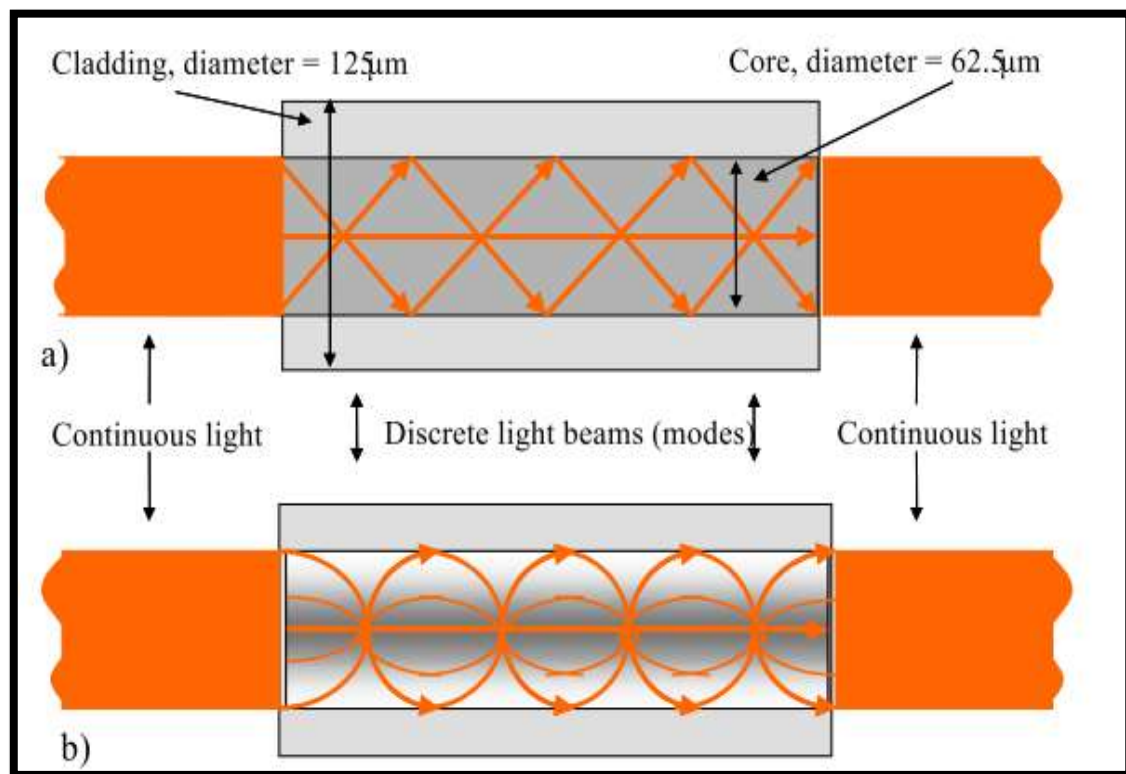


Figure (1-13) Modes in a multimode fiber:(a) Step-index MMF
(b) graded-index MMF. [84]

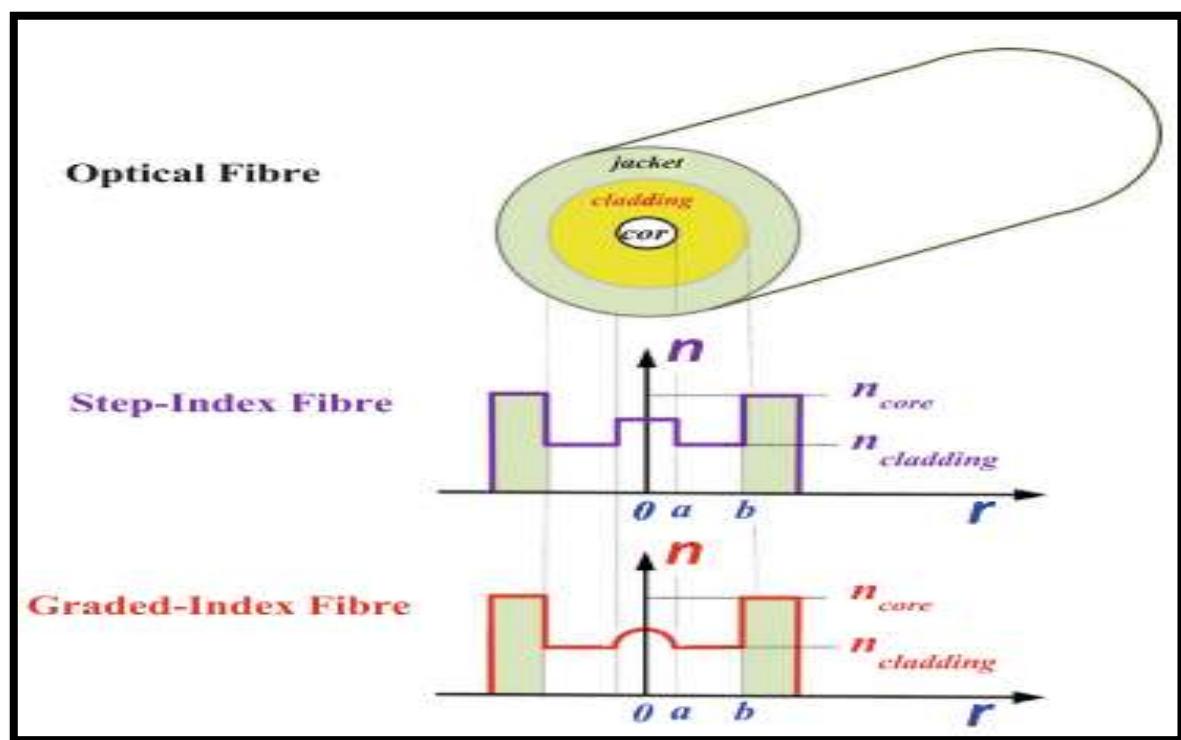


Figure (1-14) Optical fibers with step and graded index [85]

1.6.6 Evanescent waves

Evanescent Waves (EW) are a phenomenon that occurs when light has a complete internal reflection (TIR) due to the spread of electromagnetic waves through the interface between two insulators with different refractive indicators under certain boundary conditions [86]. A fade wave is created when the conditions for total internal reflection are met. Although geometric optics provides conditions for total internal reflection, they do not provide any explanation of the phenomenon or any information about the distribution of energy when reflected. The results of the electromagnetic theory should be applied to the case. The representation of the flat wave reflection at the interface is the normally polarized monochromatic flat wave of the plane [87]. At present, flammable gas sensors nowadays rely on poles, which are electric devices that detect the heat emitted when the gas oxidizes on a catalyst. The remote location of these sensors requires the installation of electrical cables, which may pose difficulties in dangerous areas. This message addresses the possibility of a fundamental form of optical fiber sensing in the middle of infrared with zirconium fluoride optical fiber. Optical sensors contain a number of attractive features such as they are immune to poisoning, perhaps more stable and selective. The sensor method examined is the interaction of the ephemeral wave with the analysis of the absorption medium) outside the fiber. This method gives direct spectral information) about the analyst. The discovered optical conveyor is modified by the absorption of guiding light due to the interaction of the ephemeral wave with the absorbed species [88]. As shown in figure (1-15)

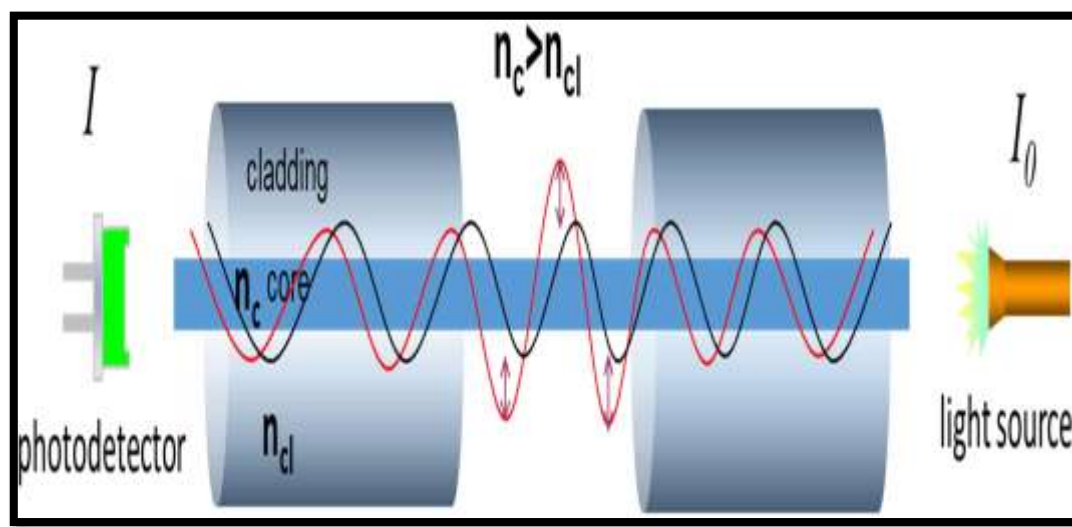


Figure (1-15) Schematic illustration of an evanescent wave based [89]

1.7 Diode laser

A diode laser is a semiconductor device that uses the p-n link for the semiconductor diode to create a coherent light and generally the length of a single wave. Because of the small volume Low energy consumption, the production of these cost-effective devices, has a diode laser Become the most common laser species in the world, used in a wide variety of components and areas, including electronics, communications, and medical practices The function of the diode laser depends on a variety of characteristics, including Current threshold, slope efficiency, and characteristic temperature. When investigating the properties of the diode laser, the plot will output the detector against the front current, known as L-I, can be used to determine the threshold Current and adoption of diode laser at different temperatures. When the data draw, the point at which a big change in the output of the detector is a signal. That the device has reached the laser conditions. The current in which this is happening is The threshold of the laser current. [90]

1.8 Literature survey

Jha Rajan et al, (2008), designed a formal interferometer based on Reflection. Use LMA PCF (24mm) long and tie it Standard SMF. The air vents have completely collapsed, allowing for the pairing and re-install the basic mode and put the cladding and use different RI, high Stability observed over time in the device. [91]

Wang and Tang (2012), designed a RI sensor using PCF. A small section of PCF (Blaze Photonics, LMA-10) From fusion paste allows basic modes and cladding to merge and Re-installation to form mach Zehnder (MZI) interferometer. They're flooded. Sensor with different concentrations of sucrose solution. [92]

Sara Jamal et.al 2015, constructed and designated a laser biosensor photonic crystal fibers (PCF) using different lengths of PCF (LMA-10) cleaved and spliced with conventional optic fiber single mode (SMF-28) for blood and urine test (hemoglobin concentration, different types of anemia, pregnancy test and general urine examination). The extreme absorbance started in the wavelengths range (470-590) nm of blood, a urine sample is in the range of (590-670) nm. The variation in the intensity (or the absorbance of a urine sample) is increased by increasing the number of biological components. The sensitivity is enlarged by increasing the length of the PCF inside the used fiber, the refractive index of the blood is improved by the increasing the level of the hemoglobin concentration, the pregnancy [93]

Rawaa and Hanan 2015, built a chemical sensor of the kind Invented by cutting and connecting single-style fibers (SMF-28) with Standard

photonic crystal fiber (PCF LM-10) at different lengths. Microscopic The collapsed area in the PCF is examined under a microscope and considered The main element of stimulating and reintegrating two key positions, they decided that interference metrics show regular interference patterns that change Note when fiber spaces are penetrated by particles Unstable vehicles and system acceptance with fast sensor information. [94]

Malath, et al in 2019. Thyroid disease can be diagnosed by measuring the body's temperature and pulse rate. Temperature and pulse rate detection is an alternative diagnostic method for the monitoring of thyroid function. A low-cost, smart sensing system to detect human relative skin temperature through non-contact and non-invasive thyroid detection methods. This is one of the simplest methods for the diagnosis of thyroid disease. The method developed tests the medical data collected and the risk value of the individual. Twelve normal subjects and eight abnormal subjects have been tested. In the case of an abnormal subject, the range of parameters exceeds the normal range. The subject is therefore considered to be a patient with thyroid disease. [95]

Shahad, et al 2019, designated and constructed optical biosensor, using three setups [photonic crystal fibers (PCF) using different lengths of PCF (LMA-10) cleaved and spliced, with conventional optic fiber single mode (SMF-28) and multimode (MMF), for detecting a different concentration of follicle-stimulating hormone (FSH), (LH) and prolactin (PRL) female hormones in the human serum, using Diode laser 450 nm. The emitted intensity measurement for all samples revealed that the concentration of the sample inversely proportional to the intensity of emission. For the LH hormone, the SMF was the best sensor in compered

with MMF and PCF. For the FSH hormone, the PCF sensor was the best in compared with SMF and MMF. [96]

Hadeel Salam, et al 2019, designed and constructed an optical biosensor, using three setups [photonic crystal fibers (PCF) using different lengths of PCF (LMA-10) cleaved and spliced, with conventional optic fiber single mode (SMF-28) and multimode (MMF), for detect concentrations ALT and AST liver enzyme, using Diode laser (532 nm). The ALT enzyme sensing in wavelength (531.62 nm) and the AST enzyme sensing in wavelength (531.16 nm) in 3 setups. The emitted intensity measurement for all samples revealed that the concentration of the sample inversely proportional to the intensity of emission. [97]



Chapter Two

Materials & Methods

2. Materials and methods

2.1 Substances, devices and Equipment

Table (2-1) Materials and Tools

Numbers	Materials and Tools	manufacturers	Country
1	Acetone 40 %		U.K.D
2	Adapter (FC Design)		China
3	Centrifuge device		Germany
4	Computer (HP)	Pavilion	China
5	Cutter		Japan
6	Diode laser (450 nm)		
7	Disposable masks and gloves	Nova	China
8	Disposable syringe 10 ml	Nova	China
9	Eppendorf tube 1.5 ml	Nova	China
10	Ethanol alcohol 96%	GSF chemical	G
11	Freezer mince 20	Panasonic	Germany
12	Gel tube 9ml	GC	America
13	Hydrofluoric acid HF 40%	HI media	Germany
14	Ice box		Germany
15	Micropipette (100- 1000) liter	Nova	Chine
16	Ocean HR2000 (Ocean Optics)		
17	Pieces of towel	Comfit	Malaysia
18	Plane tube 5m	Nova	China
19	Plastic piece		China
20	Rack of Eppendorf tube small	GC	America
21	Rack of plane tube (large)	GC	America
22	silicone adhesive		Germany

Numbers	Materials and Tools	manufacturers	Country
23	Spectrophotometer range 450 nm		
24	Sterilized cottons	Iraq	Kemadia
25	Tips of pipette 1m(blue)	Nova	China
26	Tips of pipette 1m(yellow)	Nova	China
27	Types of fibers, (single mode fiber SM-28) multimode fiber (step index)	NKT Photonic A/S	
28	Vida's device		France

2.2 Biological Sample Collection

At a Specialist Center for Endocrinology and Diabetes (SCED), Forty-five blood samples from patients, between (20 and 50) years were collected for each hormone of the thyroid (T3, T4, and TSH) and Control 15 samples. Each hormone has (15) samples from the patient and (5) sample from control, TSH samples from patient composed (2 male and 13 female) and from control (4 females, 1 male), T4 patient samples have (3 males and 12 female) and from control (3 females, 2 male), and T3 patient samples consistency from (4 males and 11 females), control samples (4 females, 1 male). As a (10 ml) of blood, in a clean dry plain plastic tube and clotting at room temperature (27°C) for 15 minutes before centrifugation. A centrifuge is done at ((5000) rpm) for a period of (5 minutes), and after the blood separation, we obtain the blood serum, and we separate the serum into two-parts equally, (5ml) is used in the traditional method to detect the concentration of thyroid hormone (T3, T4 and TSH), where they examined manually at the specialist center using Vida's, where it is an automated quantitative means test on tools used in

Vida's family, to determine the enzymatic immunity of the thyroid hormone in human serum (lithium heparin) and using ELFA fluorescent-linked enzyme assay,) Spectrophotometer at a wavelength (450) nm. The other part from serum, (5ml) used in optically detection and analysis by using a biosensor. As shown in figure (2-1).

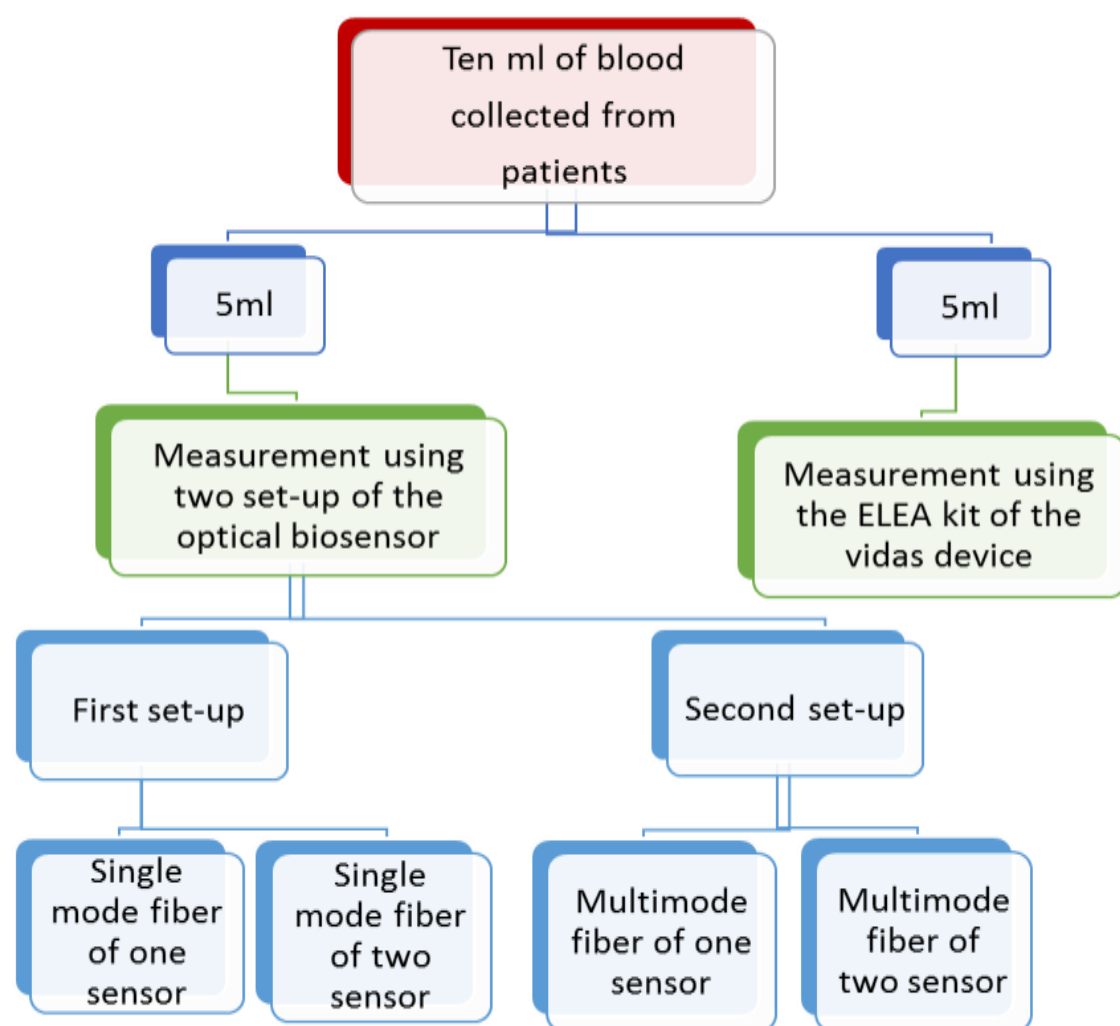


Figure (2.1) Blood Sample Collection



Figure (2-2) Tools of the Blood Sample Collection

2.3 Assessment of (T3, T4, and TSH) Levels in Serum

The serum of human blood was assessed for the level of three hormones (T3, T4, and TSH) by means of ELFA (Enzyme-Linked Fluorescent Assay) that was based on the principle of combining a one-step enzyme immunoassay sandwich method with a final fluorescent detection (ELFA). The Solid Phase Receptacle (SPR ") serves as the solid phase, as well as the pipetting device for the assay. Reagents for the assay, are ready-to-use and pre-dispensed in the sealed reagent strips. All of the assignment steps are performed automatically by the instrument. The conjugated enzyme catalyzes the hydrolysis into this substrate fluorescent product (4-Methyl-umbelliferone). The fluorescence is measuring at (450) nm and the intensity of the fluorescence is an unpaid proportional to the concentration of antigen presents in the sample and automatically calculated, then printed out at the end of the assay.

2.3.1 Methods

2.3.1.1 Measurement of Thyroid Hormones Manually

After taking the required reagents from the refrigerator and allow them to come to room temperature for at least 30 minutes. one ("TSH" or T3 or T4) strip and one (TSH" or T3 or T4) SPR for each sample were tested as control or calibrator. The test is identified by the ("TSH" or T3 or T4) code on the instrument and the calibrator must be identified by "S1", and tested in duplicate and the control was tested and identified as "C1". Then the calibrator, control, and samples were mixed using a vortex-type mixer (for serum or plasma separated from the pellet). The calibrator, control, and sample test portion is (200 ul). Note add 200 microliters from the sample serum of TSH, add 100 microliters from the sample serum of

T3, or T4 then the ("TSH" or T3 or T4) The Solid Phase Receptacle (SPR ") and ("TSH" or T3 or T4) strips inserted into the instrument. Then make the check to sure the color labels with the assay code on the SPRS and the Reagent Strips match. The assay initially directed for all steps performed automatically by the instrument. The vials Reclosed and kept to the required temperature after pipetting. The temperature of the T4 and T3 is (2-8 c).

The assay is completed within approximately 40 minutes then after the assay is completed, the SPRS and strips were removed from the instrument. Dispose of the used SPRS and strips into an appropriate recipient. was shown in figure (2-3).



Figure (2-3) the Vida's device



Figure (2-4) the test and SPRS of the Vida's device

2.4 prepare specimens for measurements using two setup of the Biosensor

The second part of blood specimens (5ml) from each patient placed in a gel tube and then separated by centrifuge for (5 minutes) for getting serum. Then this serum was divided into 4 parts in the Eppendorf tubes and Freezing at (-20°C). Then we detect and measure the hormones and its concentration by two kinds setups of the Biosensor. As shown in figure (2-5).



Figure (2-5) sample preservation tools

2.4.1 Two kinds of optical fibers were used to detect thyroid hormone (T3, T4, and TSH) concentration in the serum sample

- **Single-Mode Fiber (SMF)**

The Single-Mode Fiber (SMF) with core diameter [9 μ m] and cladding (125 μ m), fibers comprise three-coat, Core fiber made of silica with a diameter usually 9 micrometers and drugged by a substance such as germanium to raise the refractive index (RI) and pure silica cladding type

125-micron diameter and 250 mm insulator. The coating had no effect in directing the light, however, the fiber is preserved from Mechanistic damage and compromises mechanical strength.

- **Multimode Fiber (MMF)**

The diameter of the core ($55\mu\text{m}$) and the cladding ($125\mu\text{m}$) have the same manufacturing procedure as single-mode fiber. As shown in figure (2-6). Sensing of the thyroid hormone at the wavelength (450 nm) in two set-ups.

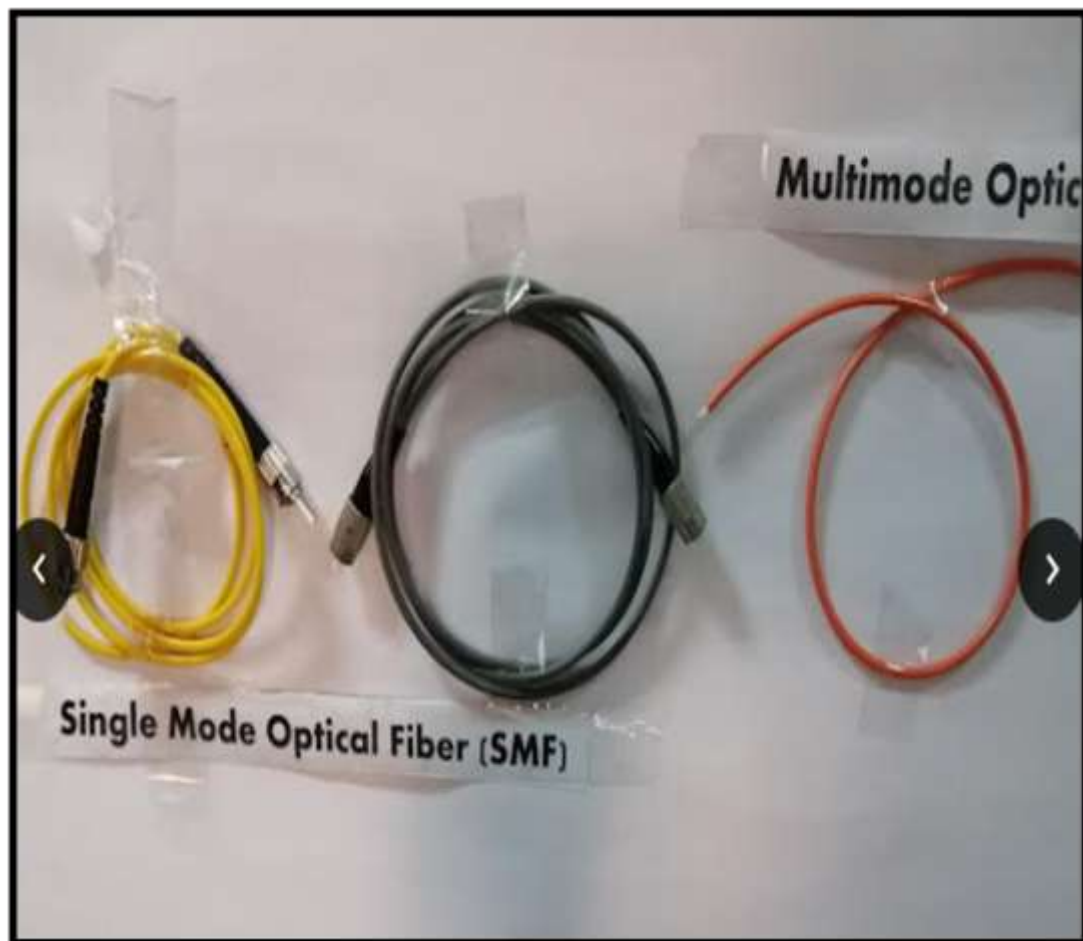


Figure (2-6) Single-Mode Fiber (SMF) and Multimode Fiber (MMF)

2.4.2 Designing an Optical Biosensor Setups

The biosensor construction of two setups (SMF1, SMF2, MMF1, MMF2). Thyroid hormones (T3, T4, TSH) are detected. This method is considered one of the newest methods.

- **Our work for detection thyroid hormones spectrally was done by following these steps.**
- **Preparing the biosensor in two setups: -**

The first setup of laser biosensor used in our study was single-mode fiber (SMF) with one sense area where the optical fiber was (30cm) length, and by using cutter a (1.5 cm) of the center of the cladding layer was removed from the fiber from each side to make a groove that we put the serum (which contain a hormone of study) in it in order to detect and measure the hormone and its concentration via the interaction of the evanescent wave of laser light with it. as shown in figure (2-7)

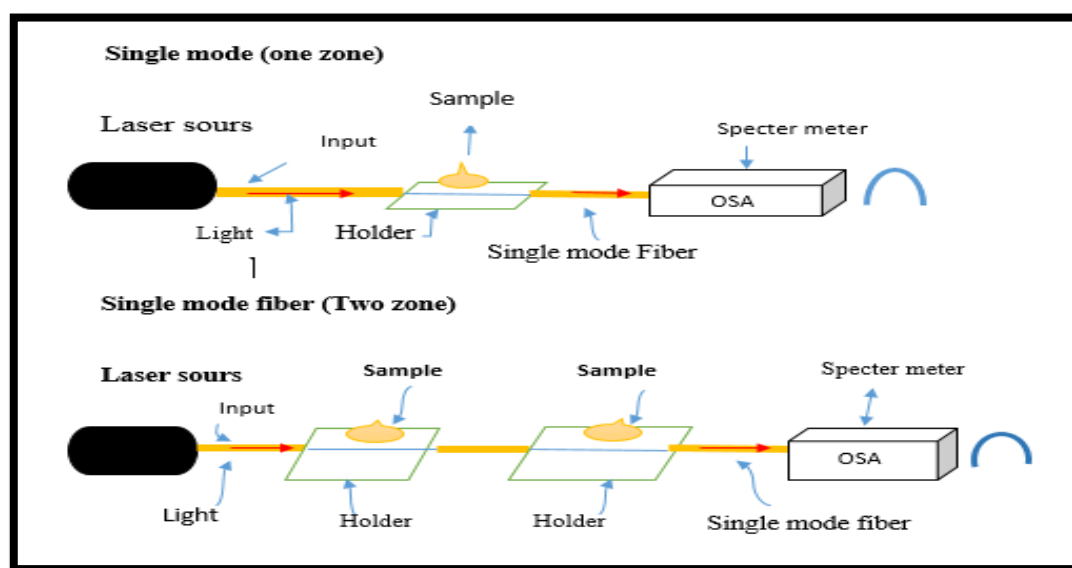


Figure (2-7) Designing of setup of single mode fiber

The other construction of optical biosensor by using single mode fiber is the same as the setup mention previously but with two holes instead of one in order to increase the sense area. The distance between these two grooves was (15 cm). as shown in figure (2-8)

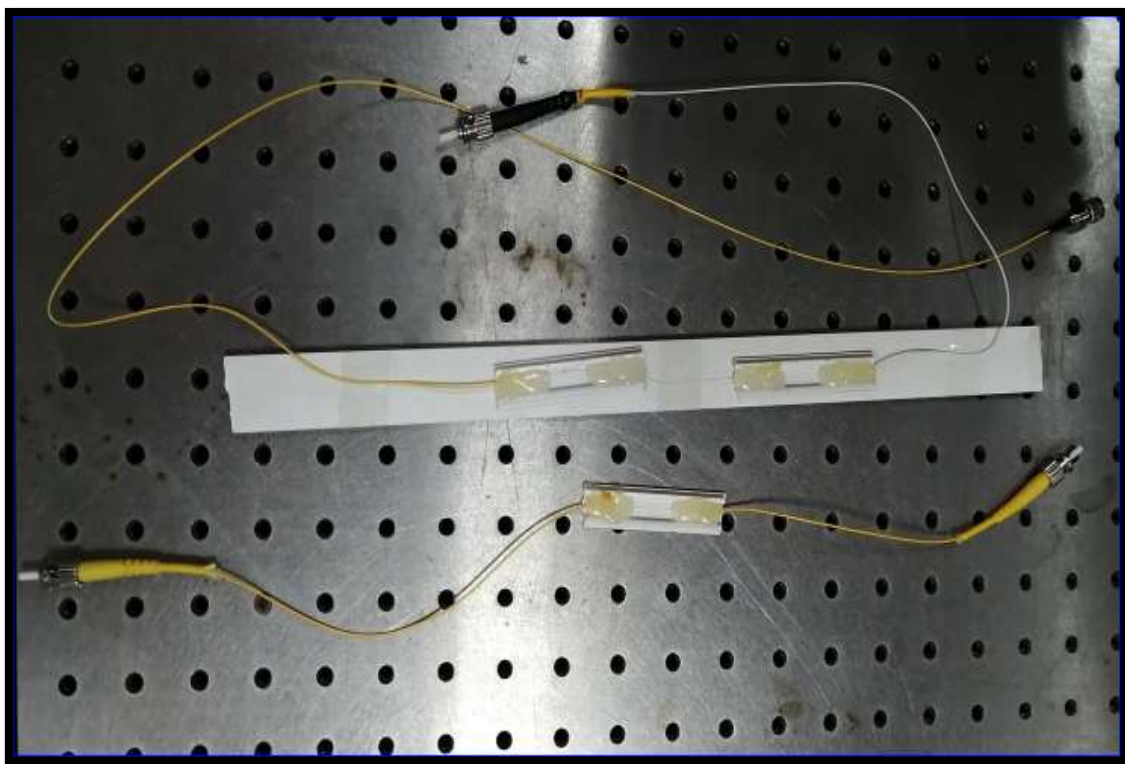


Figure (2-8) Single mode fiber (one zone and two zone)

The second setup of laser biosensor used in our study was multimode fiber (MMF) with one sense area where the optical fiber was (30cm) length, and by using cutter a 1.5 cm of the center of the cladding layer was removed from the fiber from each side to make a groove that we will put the serum (which contain a hormone of study) in it in order to detect and measure the hormone and its concentration via the interaction of the evanescent wave of laser light with it. as shown in figure (2-9)

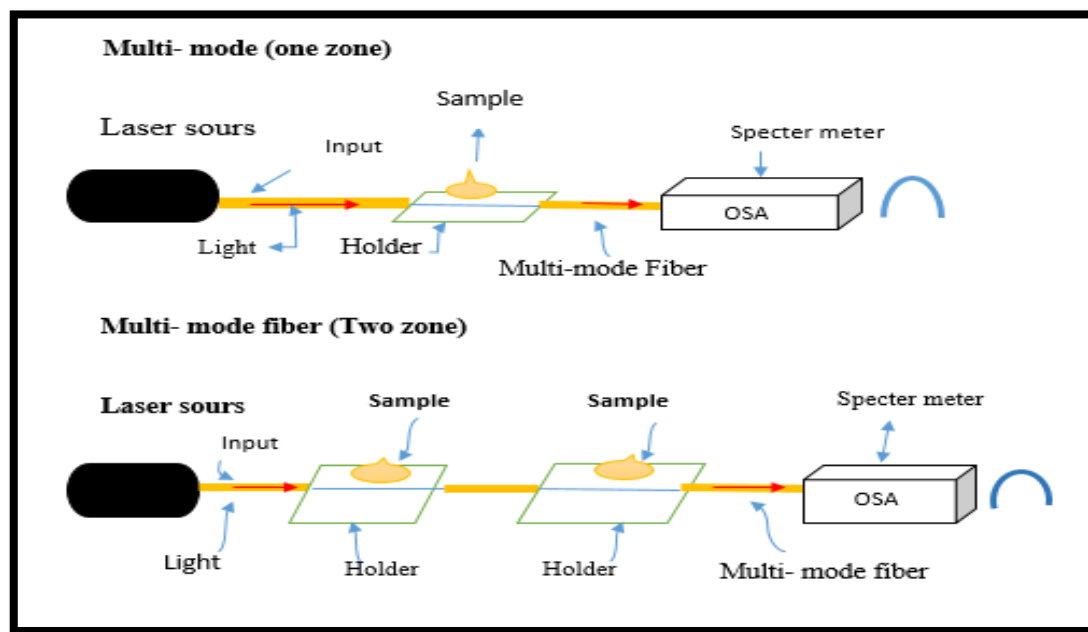


Figure (2-9) Designing of setup of Multi- mode fiber

The other construction of optical biosensor by using multimode fiber is the same as the setup mention previously but with two holes instead of one in order to increase the sensor area. The distance between these two grooves was (15 cm) as shown in figure (2-10).

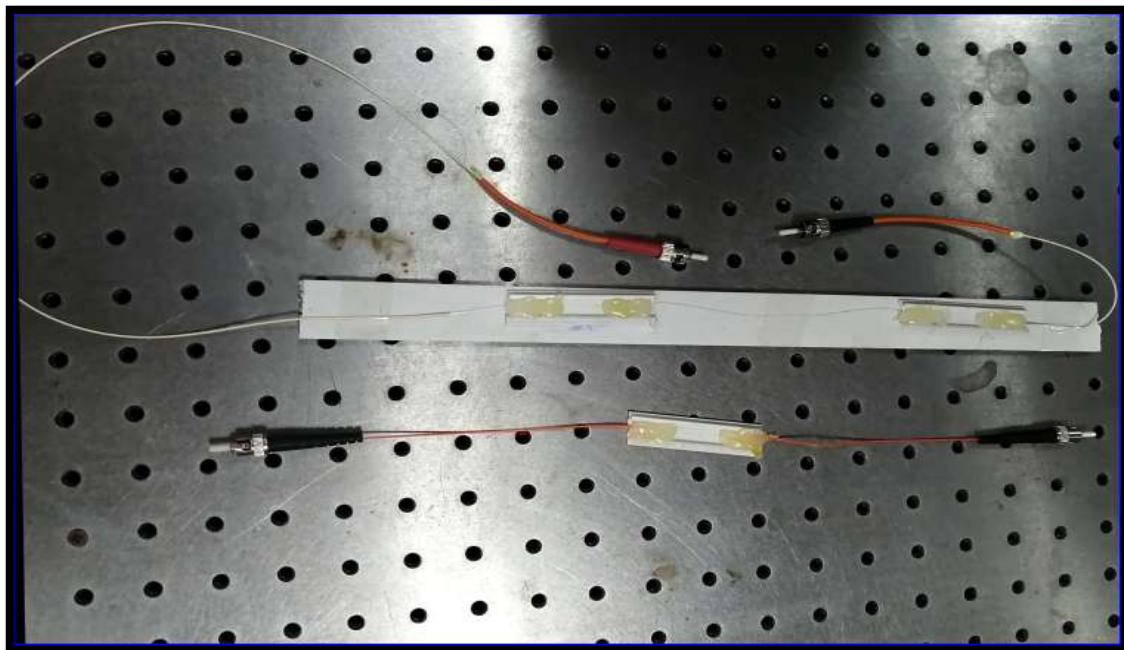


Figure (2-10) Multi- mode fiber (one zone and two zone)



Figure (2-11) tools of work

- The buffer was removed by ways of dipping the pieces in 40% acetone concentration for 30 minutes.
- Washed by distilled water. to get rid of impurities and clean it well.
- A part of the fiber is immersed in pure hydrofluoric acid (HF) 40 %. to remove the fibers cladding, in a (10-minutes) setup and then washed with distilled water. The full fibers (30 cm), was put in the aplastic device using an adhesive silicone.
- The ends of the fibers are connected to a transformer device. The terminal tools are connected to optical fibers by optical fiber connectors, such as (SC, ST, FC, LC, MTRJ, or SMA), standard connectors. Optical fibers bonded together by connectors. Splicing has been used to Join two organized fibers to form an unending optical waveguide.
- The first end was connected to a laser exporter (blue diode laser) and power supply.
- Diode laser, (450) nm wavelength, and an output power<50,000 MW was used. The Laser wavelength matches the absorption peaks of the

three thyroid hormones (T3, T4 and TSH). So it connected to a stable power supply. as shown in figure (2-8).



Figure (2-12) Diode laser.

The laser source that was used in this experiment is the blue laser with ($\lambda = 450 \text{ nm}$) and output power ($< 50000 \text{ MW}$). The laser source is powered and stable all the time of its use. This laser was selected depending on the absorption spectra of the hormones which were measured by using a spectrophotometer. Another part is connected it was a spectrum analyzer (ocean HR2000) to get an intensity signal. Optical Spectrum Analyzer (Ambient Optics HR2000) with accuracy (0.035 nm) of high wavelength and works at a wavelength of ($200\text{-}1100 \text{ nm}$), and connects the spectrometer Via a USB port or serial port to a laptop or desktop computer.

2.4.3. Spectrometer kind (Ocean Optics HR2000), has the following Features.

1-It works in the wavelength domain from (200- 1100 nm).

2-whole signal, the signal to noise ratio is (250: 1).

3-The accuracy is (0.035 nm) of high wave length.

4-Applies to (SMF, MMF). As shown in figure (2-13).

Final preparation for the placement of one mode & two mode of the sensors.



Figure (2-13) Spectrometer (HR-2000)

2.4.4 Detection of the thyroid hormones (T3, T4, and TSH) by the laser optical biosensor

The radiation of laser emitted from the laser exporter towards the spectrum analyzer inside (SMF1, SMF2, MMF1, MMF2), where the serum was put in the groove and coated all core of the fiber. The detected signal can be obtained from a spectrometer. The laser light was with wavelength (λ) 450 nm Maximum output power ($<50,000$ mW), lower large adjustment knob this exporter of laser has a power supply where is stable all the time it is used. (T3, T4, and TSH) the thyroid hormones were detected using two

setups for all setup and have its own two kinds of the fiber of the laser biosensor. As shown in figure (2-14).

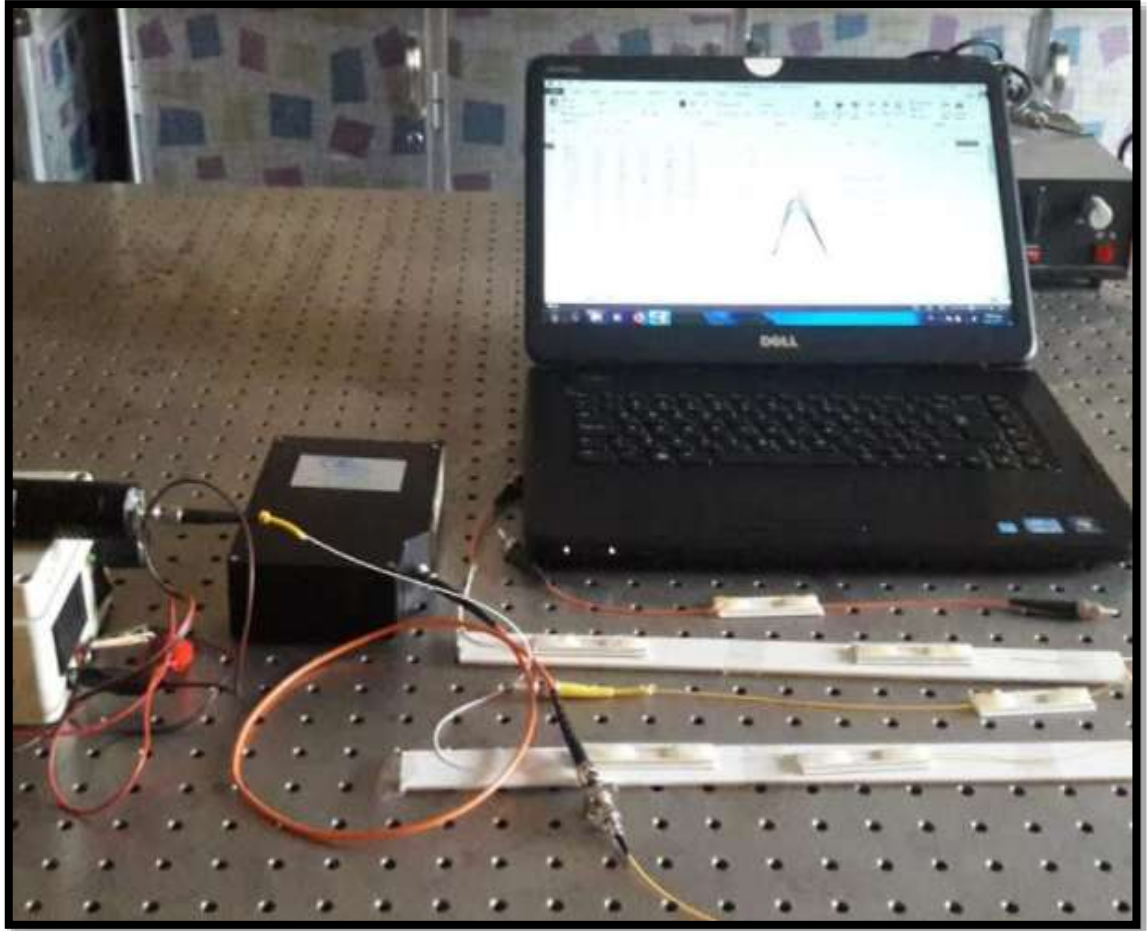


Figure (2-14) two setup of biosensor (SMF1, SMF2, MMF1.MMF2)

2.4.5 Work the test in detail in the biosensor

- The electric current was connected to the device. and the output power was less than (<50000 MW).
- Each of the accessories of the optical biosensor were connected, by an adapter. With the laser exporter from one aspect and the spectrum analyzer (ocean 2000), exemplifies the transformer and display intensity signal.
- The ($\lambda = 450$ nm) blue diode laser exporter was connected. According to the Visual properties of the standard thyroid hormones: (T3, T4, TSH). the laser exporter has a constant power exporter throughout its use. the choice of this laser source was due to the blood serum specimen absorption spectrum to this wavelength. Laser radiating from the laser exporter directed to the spectrometer, then to the inside of the fiber, to be absorbed by the blood serum specimen. To obtain spectrometer signal.
- After connecting each accessory of the optical biosensors, (0.5 ml) blood serum of the patient was added to the optical sensor (SMF1, SMF2, MMF1, MMF2) by micropipette and thereafter, the reading of the specimen intensity of the on the desktop of a computer.
- Before adding the second specimen, the sensor was cleaned from the last specimen serum used before. By washing it with distilled water and then dry it with a delicate task wiper, making sure all impurities were eliminated. Then sprinkled with alcohol. Left to dry, then add the second sample and that is how the process goes on.

2.5 Statistical Analysis

The Statistical Analysis System- SAS (2012) program was used to detect the effect of different factors in study parameters. The least significant difference –the LSD test (Analysis of Variation-ANOVA) was used to significantly compare between means. An estimate of the correlation coefficient between variables in this study. [98]

A probability value (P) is limited as:

- Non-significant at $P > 0.05$.
- Highly significant at $P \leq 0.01$.
- Significant at $P \leq 0.05$.



Chapter Three

Results & Discussion

3. Results and Discussion

3. 1 biological results

3.1.1 Measurement the Concentration of T3 hormone

Sequences results of measuring T3 hormones concentration in serum of patients' blood is stable in the table (3-1) (from higher to normal & low) concentration using the manual method by Vida's Device of the ELFA kits from 15 patients. As shown in the table (3-1) the highest focus hormone (T3) is (4.3) n mol/L, while the less focus hormone (T3) is (<0.4) n mol/L

Table (3-1) illustrate the sequence of the Concentration of the T3 hormone Measured by Vida's Device of using of the ELFA kit

Normal range T3 (0.92-2.33 n mol \L)

Numbers	Concentration of T3 n mol/L	Case
1	4.3	high
2	3.3	high
3	3.2	high
4	3.0	high
5	2.4	high
6	2.0	normal
7	1.9	normal
8	1.7	normal
9	1.5	normal
10	1.3	normal
11	0.9	low
12	0.8	low
13	0.7	low
14	<0.4	low
15	<0.4	low

3.1.2 Measurement the Concentration of T4 Hormone

Sequences results of measuring T4 hormones concentration in serum of patients' blood is stable in the table (3-2) (from higher to normal & low) concentration using manual method measurement by Vida's Device of the ELFA kits from 15 patients. Where the highest value of the T4 hormone was (175) nmoI/L, while the lowest value of hormone concentration was (16.0) nmoI/L.

**Table (3-2) illustrate the sequence of the Concentration of T4hormone Measured by Vida's Device of using of the ELFA kit
Normal range T4 (60.0-120 nmol/L)**

Numbers	Concentration of T4 n mol/L	case
1	175	high
2	172	high
3	129	high
4	128.5	high
5	123	high
6	111	normal
7	96	normal
8	92	normal
9	88	normal
10	62	normal
11	56.0	low
12	53.7	low
13	47.7	low
14	44.9	low
15	16.0	low

3.1.3 Measurement the Concentration of TSH hormone

Sequences results of measuring TSH hormones concentration in serum of patients' blood is stable in table (3-3) (from higher to normal & low) concentration using manual method measurement by Vida's Device of the ELFA kits from 15 patients. Where it shows the highest value of TSH hormone concentration was (>60.0) nmol/L, while the lowest concentration was (<0.05) nmol/L.

Table (3-3) illustrate the sequence of the Concentration of TSH hormone Measured by Vida's Device of using of the ELFA kit
Normal range TSH (0.25-5 nmol/L)

Numbers	Concentration of TSH n mol/L	Case
1	>60.0	High
2	18.5	High
3	16.6	High
4	16.5	High
5	7.4	High
6	4.3	Normal
7	3.0	Normal
8	2.3	Normal
9	1,0	Normal
10	0.7	Normal
11	0.24	Low
12	0.21	Low
13	0.10	Low
14	0.09	Low
15	<0.05	Low

3.2 Detection of T3, T4 and TSH Optically

An intensity of hormone (T3&T4 and TSH) in serum is measure optically by using two setups of laser biosensor. Both setups consist of a source of light (diode laser with 450 nm wavelength and optical fiber (single-mode (SMF) or multimode (MMF)) connected to the detector by The Adapter. However, the difference between these two setups of laser biosensor was in the number of sense area where it was one in one of them and two in another

3.2.1 Measurement of the intensity T3 hormone

The intensity of the T3 hormone of each specimen and standard is measured using two different set-ups of two sense area in (SMF setup and MMF setup) mentioned previously is tabled in a table (3-4), where the transmitted intensity arranged in ascending order from the lowest value to the highest value for each type of optical fiber using in two setups after it was sensed by the biosensor device. The spectra of the intensity of all standards and all hormone samples in two setup types of sensor fibers (SM1SM2, MM1, MM2). Vital sensors are shown in figures (3-4-A)(3-4-B)(3-4-C)(3-4-D) respectively.

Table (3-4) Shown the intensity of T3 hormone measured by biosensors.

Number	Sequence of hormone (T3) samples from (High too normal & low) Concentration of T3 n mol./L (Measured by Vida's Device)	Intensity in single mode fiber (SM1) biosensor	Intensity in single mode fiber (SM2) biosensor	Intensity in multi-mode fiber (MM1) biosensor	Intensity in multi-mode fiber (MM2) biosensor
		Mean $\pm$ SD of Intensity/ T3			
Reference	-	2425.71	1809.71	3105	3092
Standard	2ml	2803.71	2412.43	2839.71	2473.71
1	4.3	1526.86	1413.57	130914	947.143
2	3.3	1556.57	1428.57	1329	952.857
3	3.2	1652.57	1517.86	1369.14	1030.17
4	3.0	1668.57	1547.86	1381.14	1036
5	2.4	1749.71	1592.14	1393.14	1043.57
6	2.0	2464.29	1869.14	2803.71	2446.29
7	1.9	2473.71	2063.57	2841	2455.71
8	1.7	2557.71	2083.57	2900	2506.29
9	1.5	2568.86	2091.43	2919	2536.29
10	1.3	2607.43	2159.29	2938	2571.43
11	0.9	2654.57	2172.86	2958	2625.43
12	0.8	2664.86	2187.86	2979	2641
13	0.7	2674.29	2202.14	3000	2660.57
14	<0.4	2714.57	2535.43	3104	2844
15	<0.4	2785.71	2571.43	3125	2917
		2288.02 $\pm$ 126.60	1962.45 $\pm$ 98.41	2423.28 $\pm$ 202.81	2080.92 $\pm$ 206.56

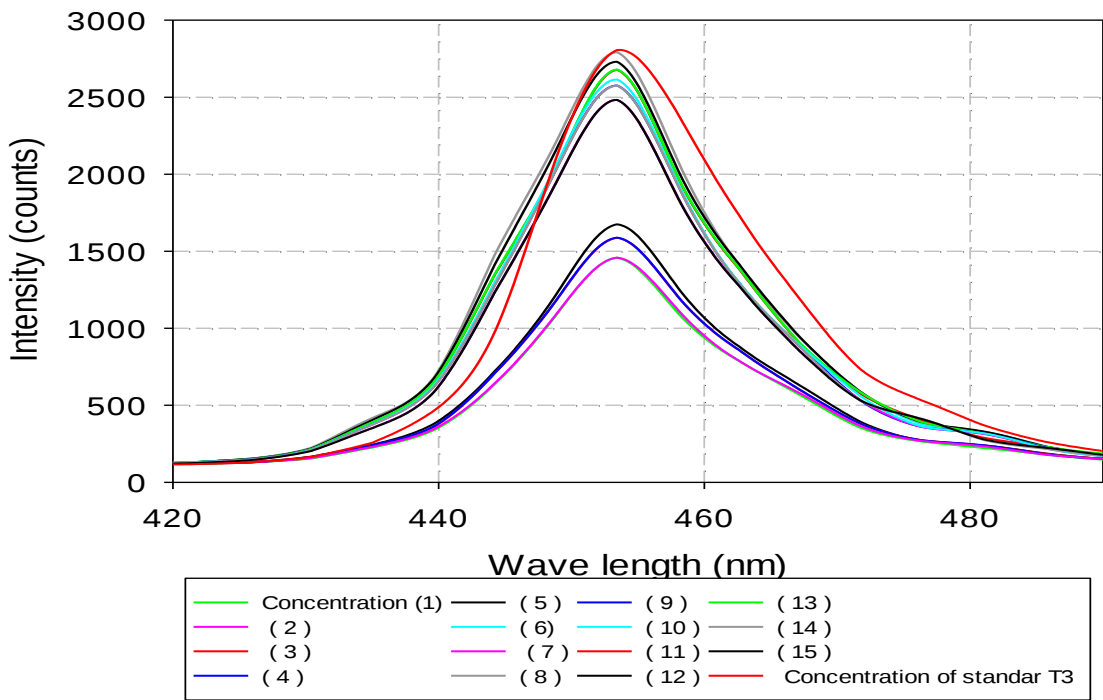


Figure (3-4-A) T3 specimen and stander Intensity peak in SMF1

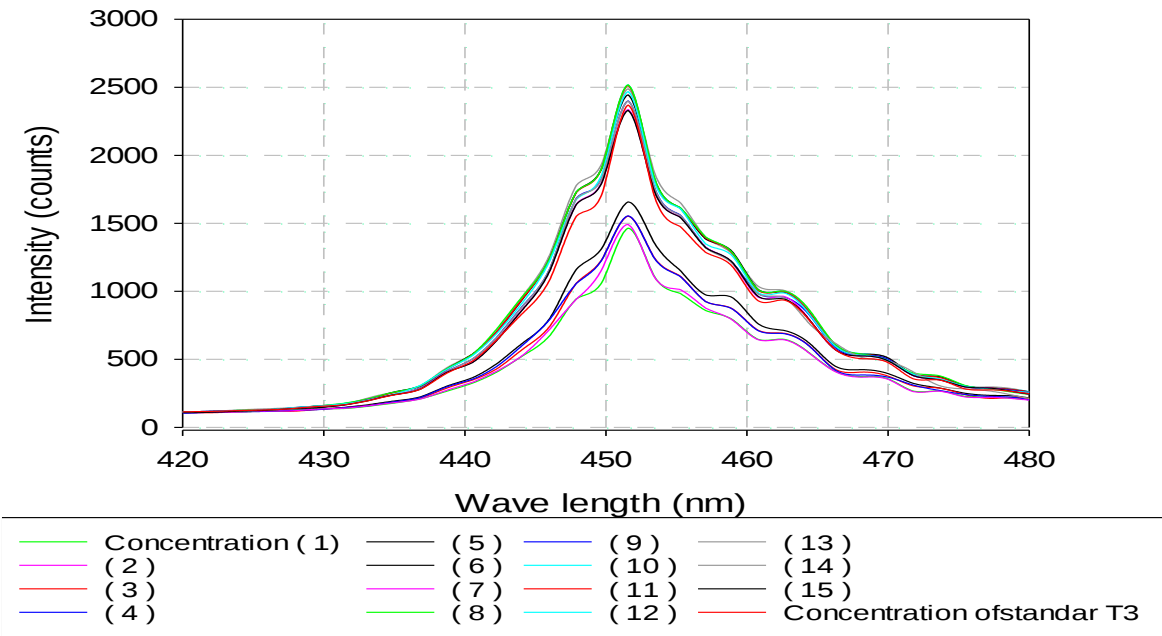


Figure (3-4-B) specimen and stander Intensity peak in SMF2

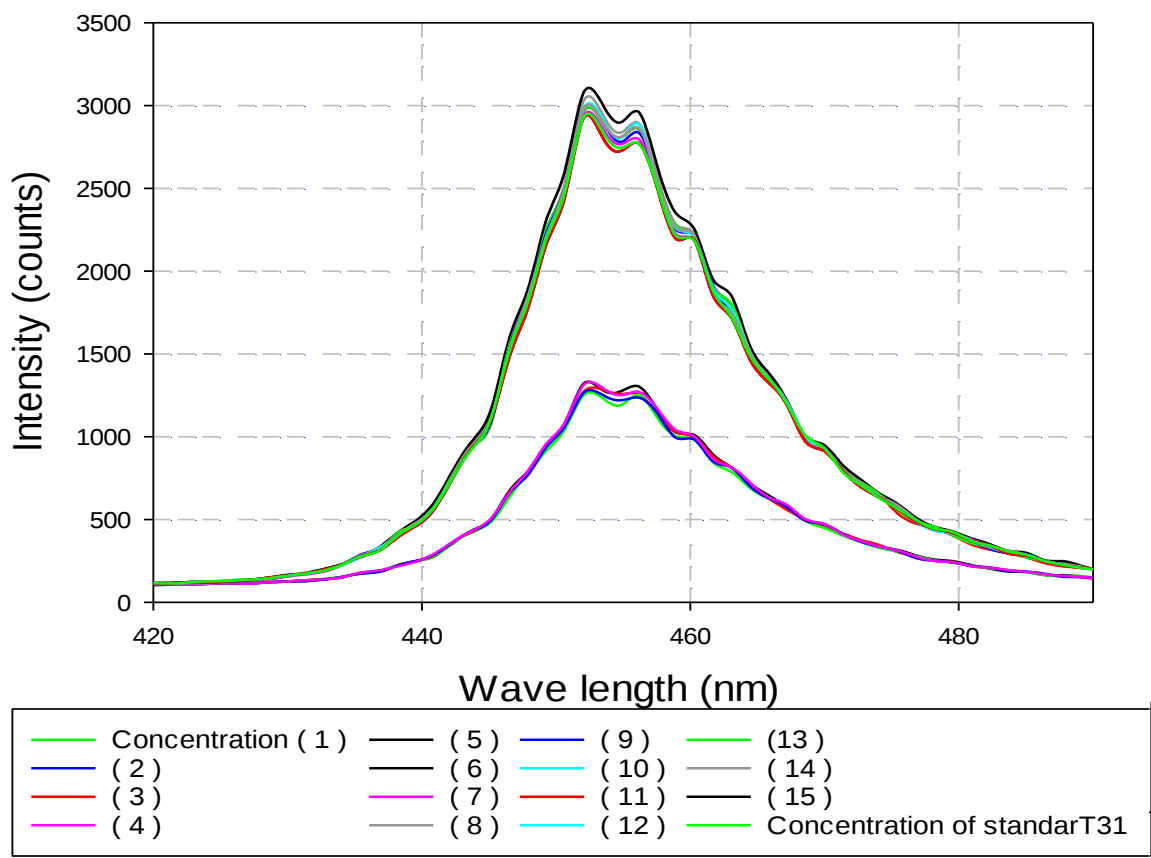


Figure (3-4-C) T3 specimen and stander Intensity peak in MMF1

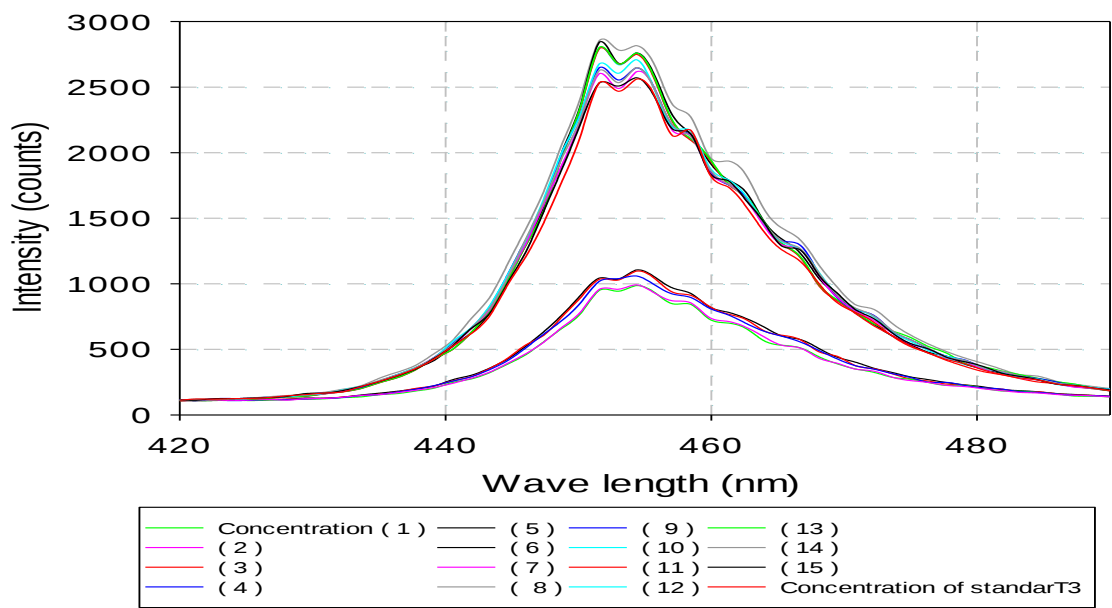


Figure (3-4-D) T3 specimen and stander Intensity peak in MMF2

3.2.2 Measurement of the intensity of T4 hormone

The intensity of T4 hormone of each specimen and standard is measured using two sets up different, the first setup has two types of optical fiber, single-mode fiber (SMF1) and multimode fiber (MMF1), both of them has one sensor, the other setup with two optical fibers, single-mode fiber (SMF2) and multi-mode fiber(MMF2) but have two sensors as shown in table (3-5). Laser sensor (1.5cm) and wavelength (450nm) have used the spectra of the T4 hormone intensity, we note as mention in table (3-4) where the intensity is arrange from the lowest value to the highest value each type of optical fiber used in two setups after it was sensed by the biosensor device. The spectra of the intensity of all standards and all hormone samples in two setup types of sensor fibers (SM1SM2, MM1, MM2). Vital sensors appear in shapes (3-5-A) (3-5-B) (3-5-C) (3-5-D) respectively

Table (3-5) Shown the intensity of T4 hormone measured by biosensors.

Number	Sequence of hormone (T4) samples from (High too normal & low) Concentration of T4 n mol./L (Measured by Vida's Device)	Intensity in single mode fiber (SM1) biosensor	Intensity in single mode fiber (SM2) biosensor	Intensity in multi-mode fiber (MM1) biosensor	Intensity in multi-mode fiber (MM2) biosensor
		Mean $\pm$ SD of Intensity/ T4			
Reference	-	2425.71	1809.71	3105	3092
Standard	4ml	2365.13	2232.14	3050	2568.86
1	175	1497.86	1399.43	1387.86	818.571
2	172	1525	1446.29	1487.86	832.857
3	129	1622.57	1534.63	1605.71	1063.57
4	128.5	1665.77	1545.43	1621.43	1080.57
5	123	1814.29	1750.29	1738.29	1154.86
6	111	2446.29	1936.43	2827.71	2336.43
7	96	2459.14	1947.86	2937	2359.29
8	92	2464.29	1949.29	2979	2393.14
9	88	2508.86	1971.43	3021	2446.29
10	62	2588.57	2023.57	3104	2607.43
11	56.0	2740.29	2299.29	3167	2696.57
12	53.7	2749.71	2306.14	3180	2749.71
13	47.7	2802.86	2365.71	3190	2767.71
14	44.9	2839.71	2426.29	3208	2785.71
15	16.0	3280	2624.57	3250	2838.86
		2333.68 $\pm$ 145.17	1968.44 $\pm$ 98.50	2580.32 $\pm$ 194.29	2062.10 $\pm$ 207.70

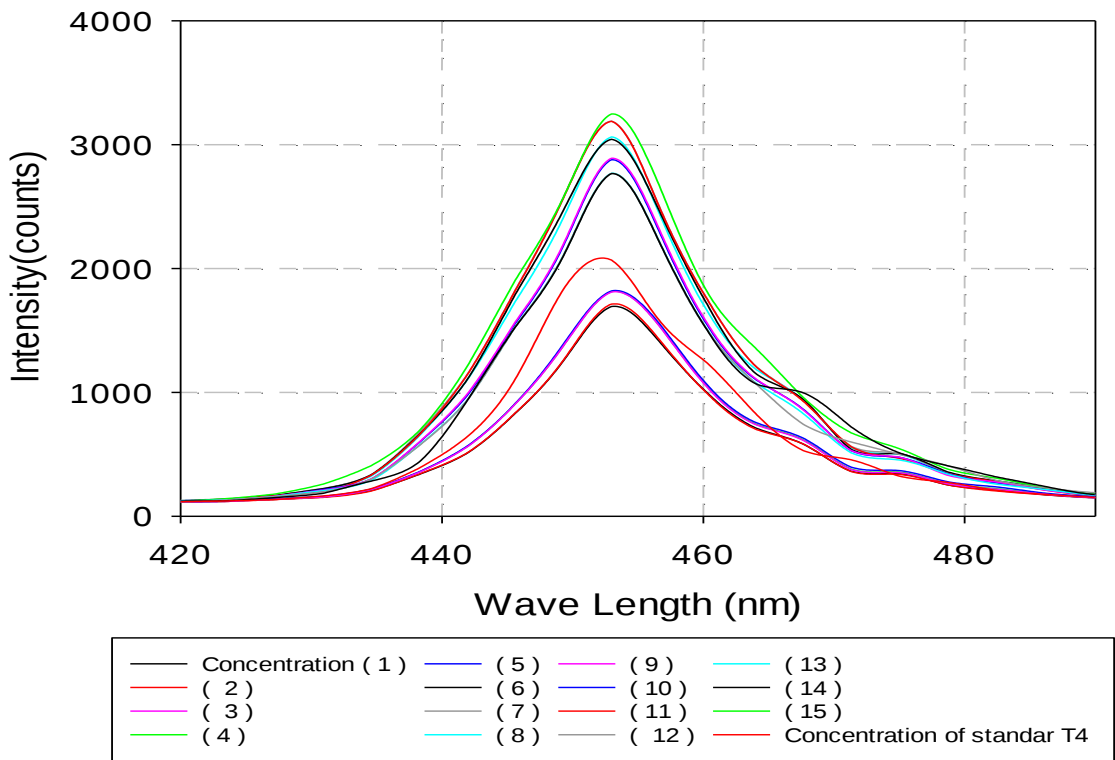


Figure (3-5-A) T4 specimen and stander Intensity peak in SMF1

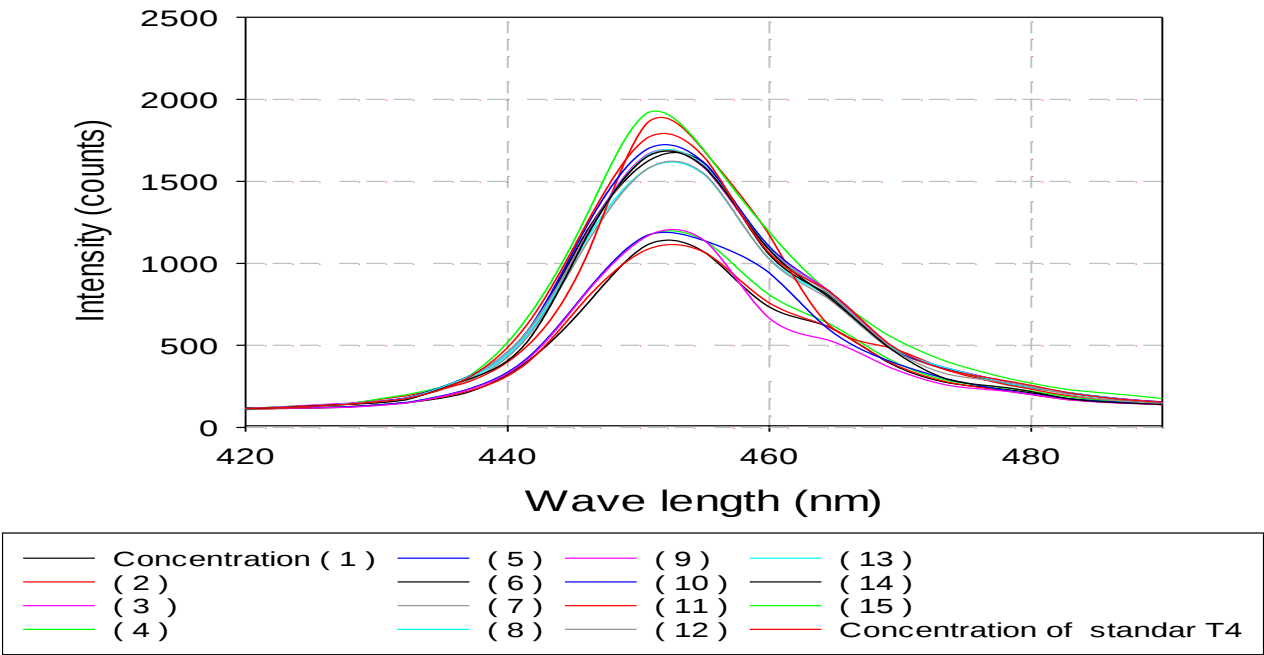


Figure (3-5-B) T4 specimen and stander Intensity peak in SMF2

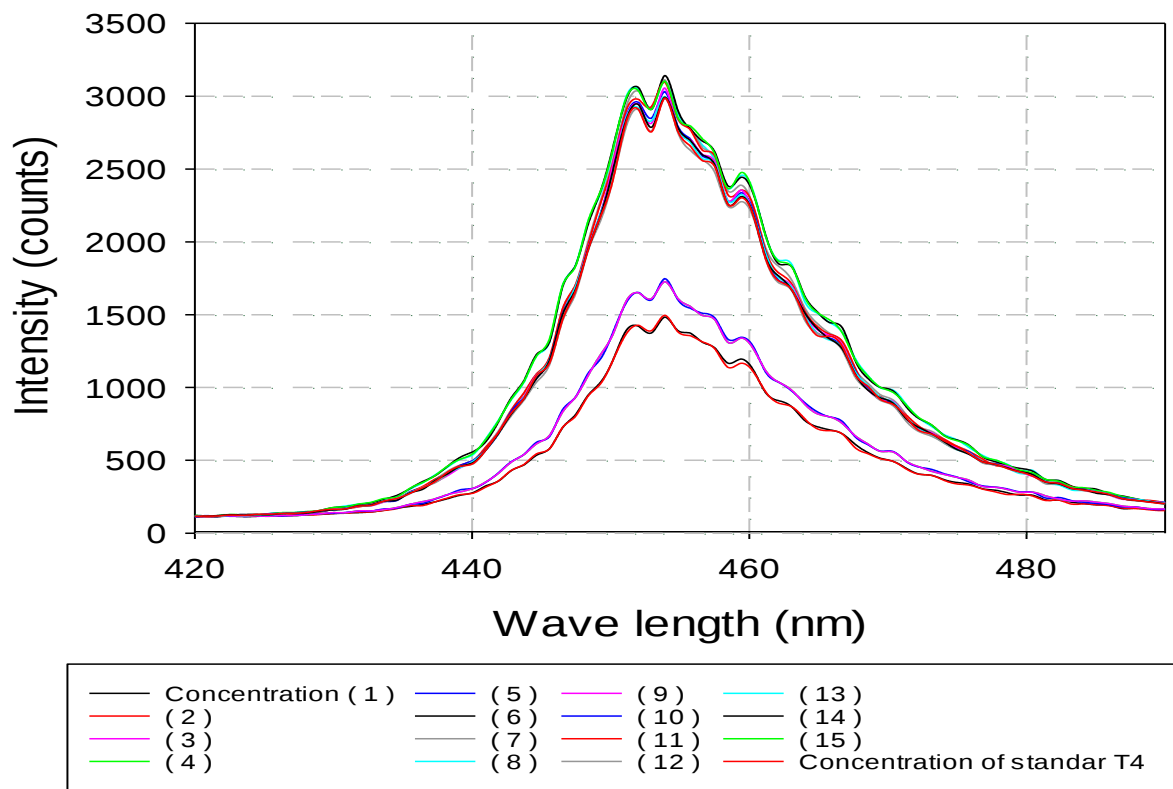


Figure (3-5-C) T4 specimen and stander Intensity peak in MMF1

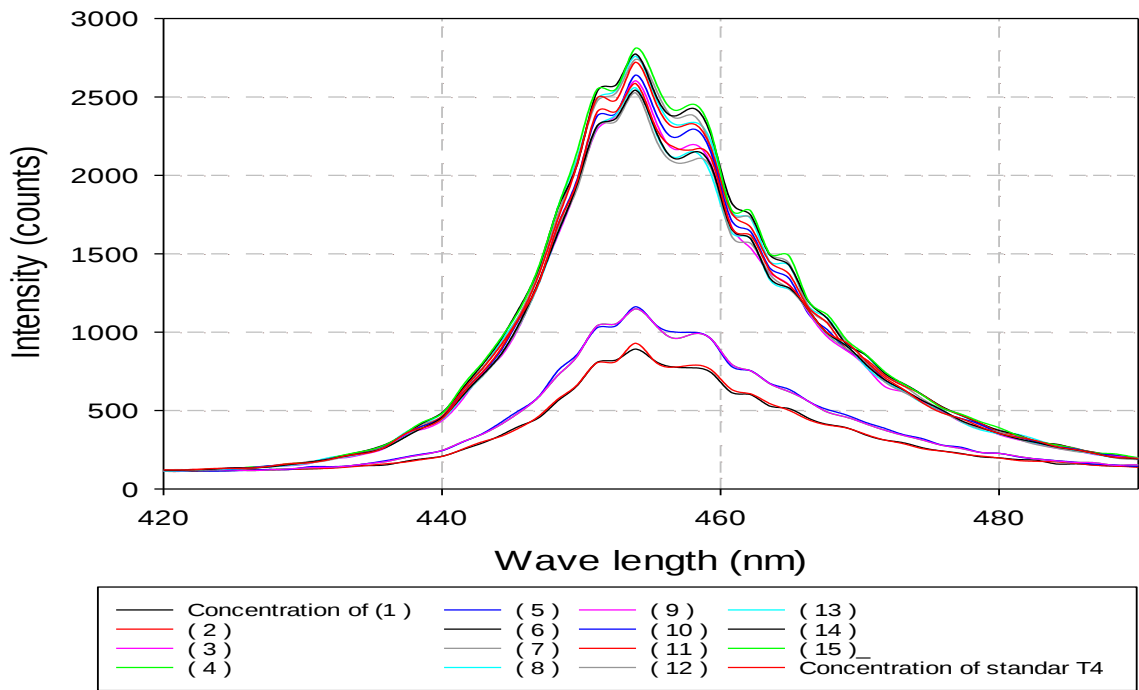


Figure (3-5-D) T4 specimen and stander Intensity peak in MMF2

3.2.3 Measurement of the intensity of TSH hormone

The intensity of TSH hormone of each specimen and standard is measured using two sets up different, the first setup with two types from optical fiber are single-mode fiber (SMF1) and multimode fiber(MMF1) both of them has one sensor, the second setup with two optical fibers are single-mode fiber (SMF2) and multi-mode fiber(MMF2) both of them has two sensors as shown in table (3-6). Laser sensor of (1.5cm) length and wavelength (450nm) were used the spectra of the TSH hormone intensity, we note in the table (3-4). The intensity arranged from the lowest value to the highest value each type of optical fiber used in two setups after it sensed by the biosensor device. The spectra of the intensity of all standards and all hormone samples in two setup types of sensor fibers (SM1SM2, MM1, MM2). Vital sensors appear in shapes (3-6-A) (3-6-B) (3-6-C) (3-6-D) respectively.

Table (3-6) Shown the intensity of TSH hormone measured by biosensors.

Number	Sequence of hormone (TSH) samples from (High too normal & low) Concentration of TSH n mol./L (Measured by Vida's Device)	Intensity in single mode fiber (SM1) biosensor	Intensity in single mode fiber (SM2) biosensor	Intensity in multi-mode fiber (MM1) biosensor	Intensity in multi-mode fiber (MM2) biosensor
		Mean $\pm$ SD of Intensity/ TSH			
Reference	-	2425.71	1809.71	3105	3092
Standard	2 ml	2446.872	2345.71	3480	2797
1	>60.0	1463.0	1153.57	1479	1100
2	18.5	1776.0	1377.14	1694.29	1276.43
3	16.6	1785.71	1380.0	1714.29	1340
4	16.5	1797.71	1387.43	1732.57	1460.71
5	7.4	2029.71	1421.43	1762.29	1637
6	4.3	2172.14	2081.14	3261	2771.14
7	3.0	2217.14	2090.71	3292	2803.17
8	2.3	2237.14	2129.14	3305	2832.26
9	1,0	2276.43	2142.86	3394.29	2892
10	0.7	2356.43	2157.86	3420.57	3020
11	0.24	2780.57	2268.0	3428.57	3043
12	0.21	2782.29	2299.29	3435	3062
13	0.10	2791.71	2321.43	3649.29	3218
14	0.09	2797.0	2327.14	3666.29	3124
15	<0.05	2811.43	2387.14	3690.29	3229
		2271.63 $\pm$ 115.42	1928.29 $\pm$ 113.80	2861.65 $\pm$ 226.95	2453.91 $\pm$ 210.92

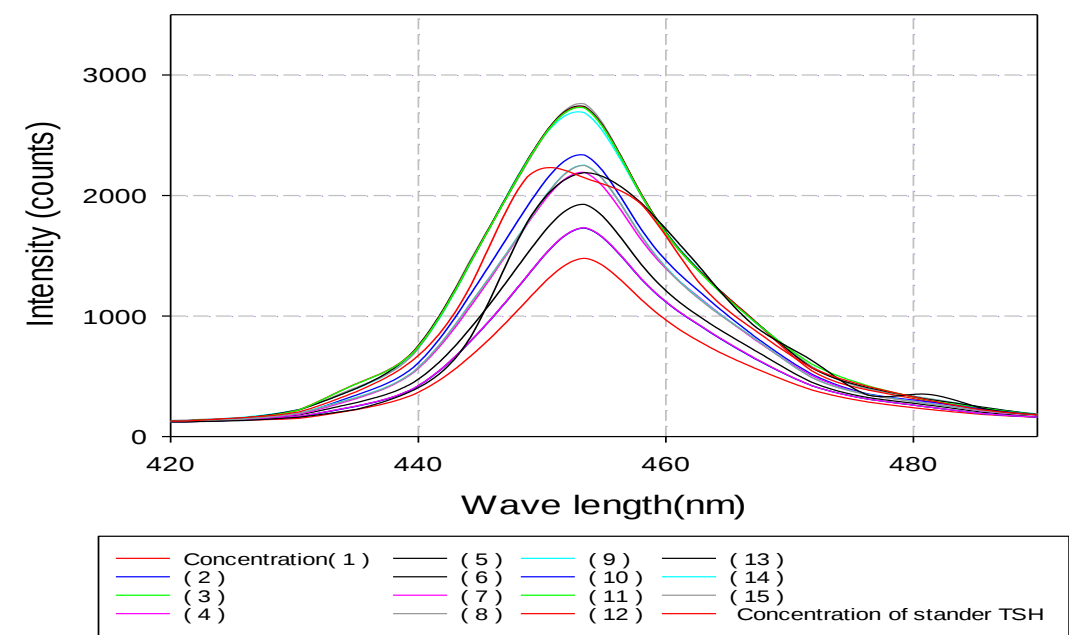


Figure (3-6-A) TSH specimen and stander Intensity peak in SMF1

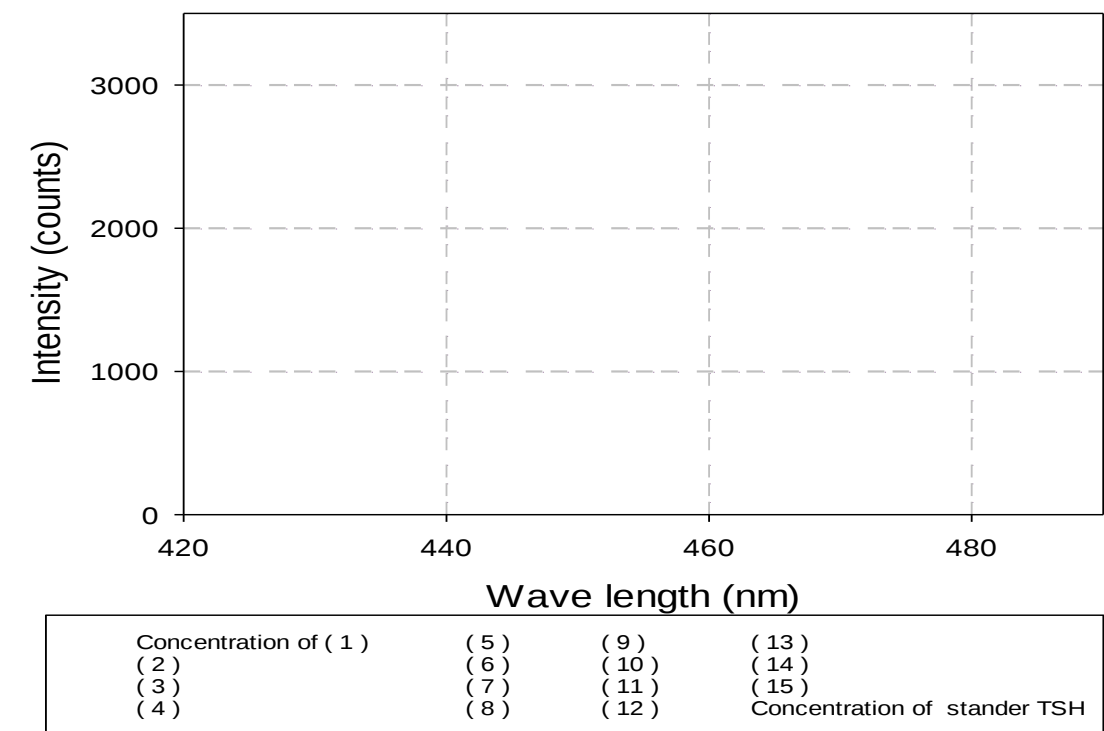


Figure (3-6-B) TSH specimen and stander Intensity peak in SMF2

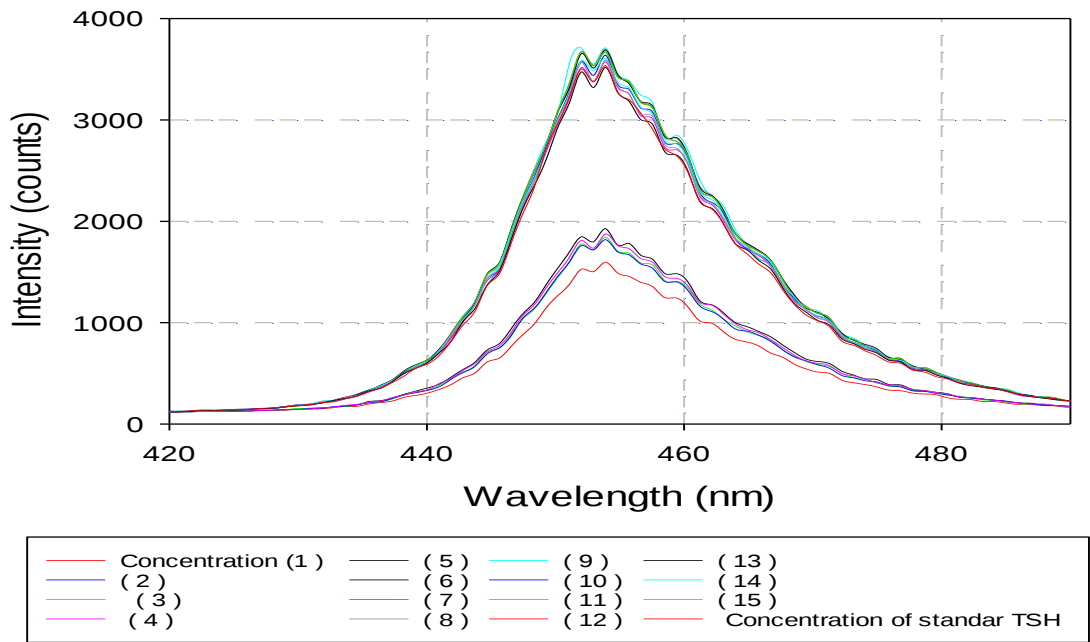


Figure (3-6-C) TSH specimen and stander Intensity peak in MMF1

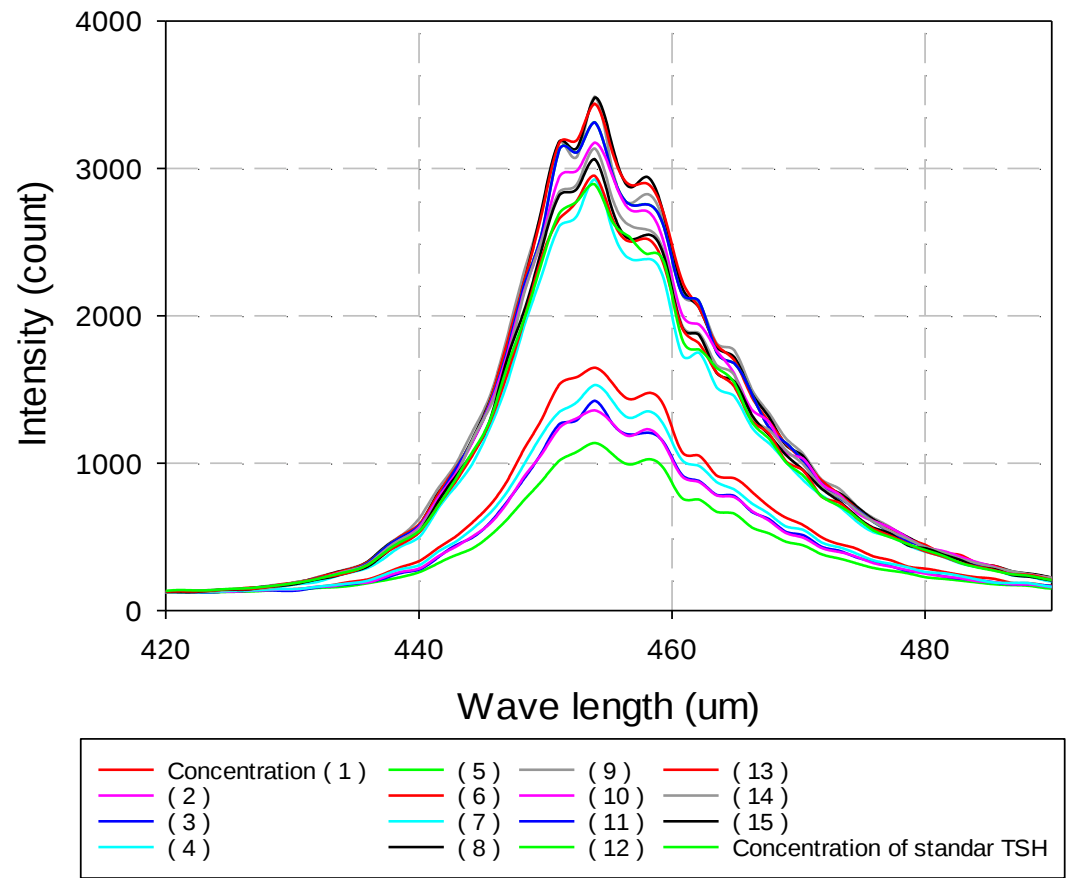


Figure (3-6-D) TSH specimen and stander Intensity peak in MMF2

3.3 Statistical Result

The display of results of the data analysis in figures and tables explaining in the present partition for detection of the thyroid hormones (T3&T4 and TSH) and as follows: -

3.3.1 Statistical Analysis

The Statistical Analysis System- SAS (2012) program was using to detect the effect of difference factors in study parameters. Least significant difference – the LSD test (Analysis of Variation-ANOVA) was used to significant compare between means. Estimate of correlation coefficient between variables in this study.

A probability value (P) is limited as:

- 1- Non-significant at $P > 0.05$.
- 2- Highly significant at $P \leq 0.01$.
- 3- Significant at $P \leq 0.05$.

3.3.1.1 Triiodothyronine (T3)

The result of this study showed that the mean $\pm$ SD values of the measured between SMF1 (2288.02 ± 126.60) biosensor, SMF2 biosensor (1962.45 ± 98.41), MMF1 biosensor (2423.28 ± 202.81) and MMF2 biosensor (2080.92 ± 206.56) were Non-Significant. AS shown in table (3-7)

Table (3-7) Comparison between difference groups in Intensity of the hormone T3 using Biosensors

Group	Number of samples	Mean $\pm$ SD of Intensity/ T3
Single mode fiber (SMF1) biosensor	15	2288.02 $\pm$ 126.60
Single mode fiber (SMF2) biosensor	15	1962.45 $\pm$ 98.41
Multi-mode fiber (MMF1) biosensor	15	2423.28 $\pm$ 202.81
Multi-mode fiber (MMF2) biosensor	15	2080.92 $\pm$ 206.56
LSD value	---	468.76 NS
P-value	---	0.210
NS: Non-Significantly.		

Results show due to mean values that T3 hormone of using (MMF1) different parameters technique has accounted for the high-intensity level, then followed by (SMF1) technique, and (MMF2) technique finally by (SMF2) technique, which has recorded the low mean value. In addition to that, the T3 hormone of using (MMF1) technique has accounted for the high-intensity level the laser diode blue, followed by (SMF1 and MMF2) technique, and finally by (SMF2) technique. From the previous results, it could be summarize that the T3 hormone of using the MMF1 technique has accounted for the high-intensity level, while the SMF2 technique, has recorded the lowest mean value in relative, shown in Figure (3-7).

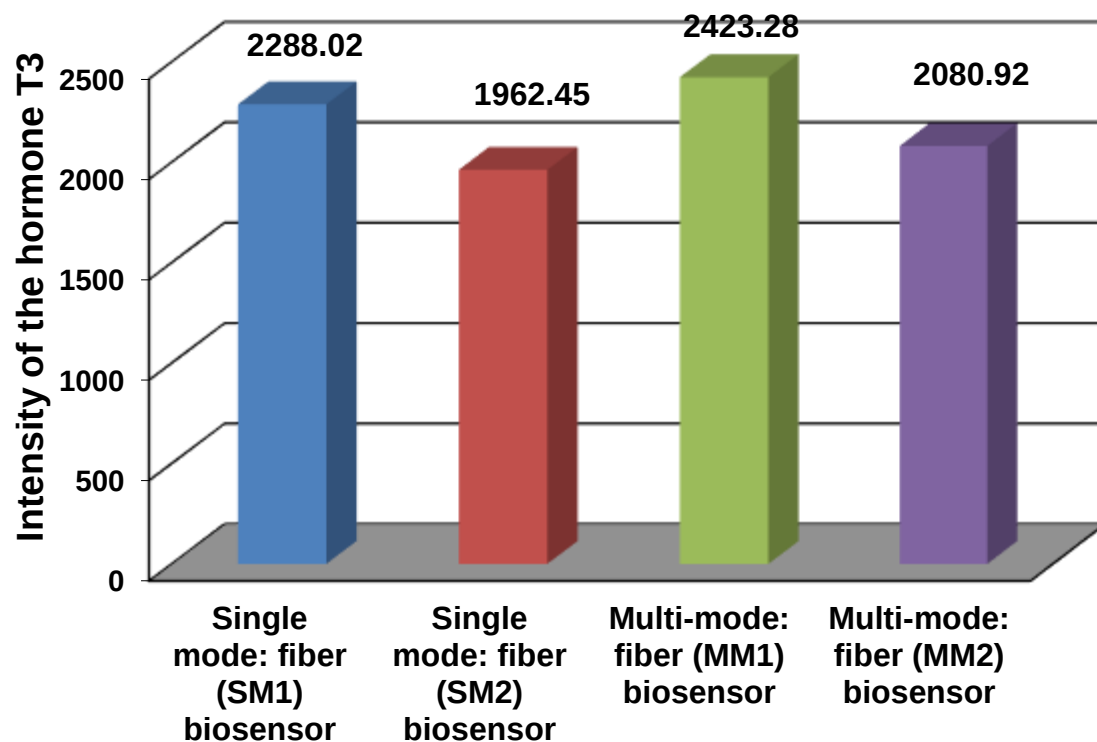


Figure (3-7) Comparison between difference groups in Intensity of the hormone T3 using biosensors

The results of this study showed a highly significant ($p \leq 0.01$) decrease in the T3 Correlation coefficient between concentration and Intensity.as shown in table (3-8). In table (3-8). Inversely proportional between Parameters and correlation coefficient-r with a concentration.

Table (3-8) Correlation coefficient between Focus and Intensity of T3

Parameters	Correlation coefficient-r with concentration	P-value
Single mode fiber (SM1) biosensor	-0.93 **	0.0001
Single mode fiber (SM2) biosensor	-0.96 **	0.0001
Multi-mode fiber (MM1) biosensor	-0.89 **	0.0001
Multi-mode fiber (MM2) biosensor	-0.91 **	0.0001
** ($P \leq 0.01$) H. Sig.		

3.3.1.2 Thyroxine (T4)

The results of this study showed a mean $\pm$ SD of intensity between SMF1 (2333.68 ± 145.17), SMF2 (1968.44 ± 98.50), MMF1 (2580.32 ± 194.29) and MMF2 (2062.10 ± 207.70) were significantly ($p \leq 0.05$). AS shown in table (3-9)

Table (3-9): Comparison between difference groups in Intensity of the hormone T4 using Biosensors

Group	Number of sample	Mean $\pm$ SD of Intensity/ T4
Single mode fiber (SMF1) biosensor	15	2333.68 ± 145.17 ab
Single mode fiber (SMF2) biosensor	15	1968.44 ± 98.50 b
Multi-mode fiber (MMF1) biosensor	15	2580.32 ± 194.29 a
Multi-mode fiber (MMF2) biosensor	15	2062.10 ± 207.70 b
LSD value	---	473.34 *
P-value	---	0.0414
Means having with the different letters in same column differed. * ($P \leq 0.05$ significantly).		

Results show due to mean values that T4 hormone of using MMF1 different parameters technique has accounted for the high-intensity level, and then followed by (SMF1) technique, and (MMF2) technique finally by (SMF2) technique, which has recorded the low mean value. In addition to that, the T4 hormone of using (MMF1) technique has accounted for the high-intensity level of the laser diode blue, followed by (SMF1 and MMF2) technique, and finally by (SMF2) technique. From the previous results, it could be summarize that the T4 hormone of using the MMF1 technique has accounted for the high-intensity level, while the SMF2 technique, has recorded the lowest mean value in relative, shown in Figure (3-9).

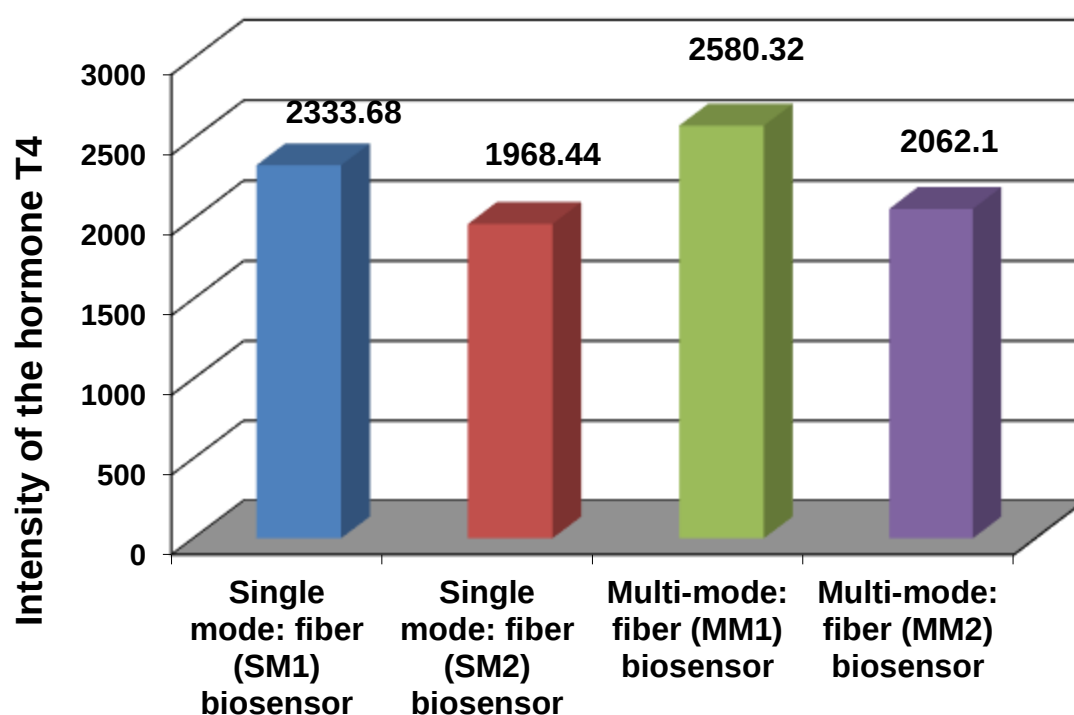


Figure (3-9) Comparison between difference groups in Intensity of the hormone T4 using biosensors

The results of this study showed a highly significant ($p \leq 0.01$) decrease in the T4 Correlation coefficient between concentration and Intensity.as shown in table (3-10). In the table (3-10). inversely proportional between Parameters and correlation coefficient-r with a concentration.

Table (3-10) Correlation coefficient between Focus and Intensity of T4

Parameters	Correlation coefficient-r with concentration	P-value
Single mode fiber (SM1) biosensor	-0.95 **	0.0001
Single mode fiber (SM2) biosensor	-0.97 **	0.0001
Multi-mode fiber (MM1) biosensor	-0.90 **	0.0001
Multi-mode fiber (MM2) biosensor	-0.92 **	0.0001
** ($P \leq 0.01$)- H. Sig.		

3.3.1.3 Thyroid-stimulating hormone (TSH)

The results of this study showed a mean $\pm$ SD of intensity between SMF1 (2271.63 ± 115.42), SMF2 (1928.29 ± 113.80), MMF1 (2861.65 ± 226.95) and MMF2 (2453.91 ± 210.92) were significantly ($p \leq 0.01$). AS shown in table (3-11)

Table (3-11) Comparison between difference groups in Intensity of the hormone TSH using Biosensors

Group	Number of samples	Mean $\pm$ SD of Intensity/ TSH
Single mode fiber (SM1) biosensor	15	2271.63 ± 115.42 bc
Single mode fiber (SM2) biosensor	15	1928.29 ± 113.80 c
Multi-mode fiber (MM1) biosensor	15	2861.65 ± 226.95 a
Multi-mode fiber (MM2) biosensor	15	2453.91 ± 210.92 ab
LSD value	---	495.31 **
P-value	---	0.0041
Means having with the different letters in same column differed significantly. ** ($P \leq 0.01$).		

Results show due to mean values that TSH hormone of using MMF1 different parameters technique has accounted for the high-intensity level, and then followed by (MMF2) technique and (SMF1) finally by (SMF2) technique, which has recorded the low mean value. In addition to that, the TSH hormone of using (MMF1) technique has accounted for the high-intensity level, followed by (MMF2 and SMF1) technique and finally by (SMF2) technique. From the previous results, it could be summarize that the TSH hormone of using the MMF1 technique has accounted for the high-intensity level, while the SMF2 technique, has recorded the lowest mean value in relative, shown in Figure (3-11).

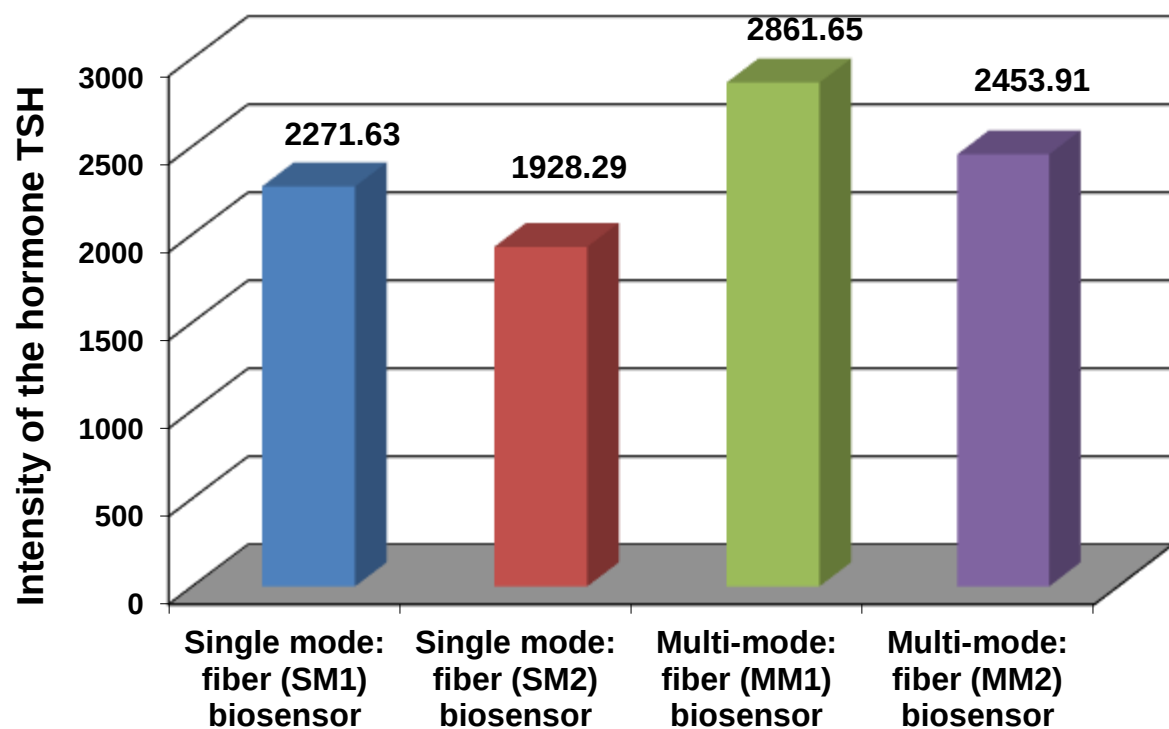


Figure (3-11) Comparison between difference groups in Intensity of the hormone TSH using biosensors

The results of this study showed a highly significant ($p \leq 0.01$) decrease in the TSH Correlation coefficient between concentration and Intensity.as shown in table (3-12). In the table (3-12). Inversely proportional between Parameters and correlation coefficient-r with a concentration.

Table (3-12) Correlation coefficient between Focus and Intensity of TSH

Parameters	Correlation coefficient-r with concentration	P-value
Single mode fiber (SM1) biosensor	-0.78 **	0.0010
Single mode fiber (SM2) biosensor	-0.78 **	0.0009
Multi-mode fiber (MM1) biosensor	-0.74 **	0.0022
Multi-mode fiber (MM2) biosensor	-0.77 **	0.0012
** (P≤0.01)-H. Sig.		

3.4 Discussions

The current study including the uses optically biosensor system for detection of the thyroid hormones in the blood serum. A biosensor is a device that measures chemical reactions and biological generating signals that matching focusing the analyzer in the reaction. Two setups were using for detection setup of the thyroid hormone, the first setup (single mode and multimode of one sensor) the second setup is (single mode and multimode of two sensor). The result shows that the first setup of multimode is better the other setups for detection, (Shahad, et al 2019), detection female hormones (LH & FSH and PRL) by using a diode laser (blue) at a wavelength (450 nm), that agree with our study's results [96]. Using Lasers with different wavelengths for different biological applications such as blood and urine tests, based on Mach-Zehnder interferometer laser with (532nm) as a laser source with an input power of (12.2 nw). A laser biosensor is designed with different lengths of solid-core photonic crystal fibers (LMA-10) (1.5cm, 1cm, and 0.5cm) to be used for the detection of different types of anemia such as iron deficiency and aplastic anemia, the device with the hole collapsed, the LMA-10 photonic crystal fiber was spliced by fusion splicer type (FSM 60 S) to the SMF-28. A collapsing technique can be implement in this sensor. PCF sensor used with length (1.5cm) because it proved to be the most sensitive sensor for changing the refractive index of the biological. The light green source laser has been used in this experiment with ($\lambda=532\text{nm}$) and output power = (12.2nw) [93]. The results shows that the first setup of multimode is better that other setup for detection of T3 hormone was (2423.28 ± 202.81), the result of the T4 hormone in multimode MMF1 was (2580.32 ± 194.29). The result of TSH hormone in multimode MMF1 (2861.65 ± 226.95). Therefore, multimode

(MMF1) is best comparing with than single mode because the core of multimode is larger than the core of single mode. When we comparing a multimode of one sensor area with a multimode of two sensors area, we found that the multimode of one sensor is better that the multi-mode of two sensors area for detection all hormones. When the area is increased, the sample size will be increased or doubled, that means one sensor will take (0.5 ml) of blood serum from the sample. While two sensors will take (1 ml) of serum. The light absorption highly by the higher concentrated of hormones and this causes lower transmitted intensity. In addition, this resulting from highly matching between the sample and wavelength of the light (source of light biosensor system) , finally we reach to that, the optical biosensor is more effective, more stabilized, sensitive, cheaper method for detection the thyroid hormone from the ordinary method.

3.5 Conclusions

The current study is getting on the following conclusion concerning the outcomes obtained through the experiment.

1. The MMF1 was the better sensor compared with (SMF1, SMF2, and MMF2).
2. The emitted intensity measurement for all samples revealed that the concentration of the sample inversely proportional to the intensity of emission.
3. The biosensor is the most currents with quick diagnosis, and this way is more expensive than the traditional way. Any biologic changes in the specimen, such as blood that lead to radical optical changes in (absorption and refractive) of the blood specimen.

3.6 Recommendations

Detection of the kinds of other hormones such as growth hormone

- 1- Growth Hormone (GH) from the somatotrophs,
- 2- Prolactin from the lactotrophs,
- 3- Adrenocorticotrophic hormone (ACTH) from the corticotrophs.
- 4- Detection of any biological specimen such as viruses or bacteria.
- 5- Different type of laser.



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الخلاصة

الهرمونات هي ناقل كيميائي له تأثيرات تنظيمية محددة على أعضاء أو خلايا معينة. وظيفتها تنظيم النمو والتمثيل الغذائي والتكاثر وردود الفعل الأخرى. يتم استخدام ثلاثة أنواع من الهرمونات في هذا العمل وهي هرمونات الغدة الدرقية (تحفيز الغدة الدرقية (TSH) وثيروكسين (T4) وثلاثي يودوثيرونين (T3)) حيث تم قياسها بالطريقة العادية مثل Vida للقياس الكمي لإجمالي و باستخدام ELFA (المقاييس الفلوري المرتبط بالإنزيم) وغيرها التي كانت باهظة الثمن وتتطلب وقتًا وجهدًا. لذلك فكرنا في استخدام طريقة جديدة للكشف عن هذه الهرمونات بصريًا وهي أكثر دقة ووقتًا أقل وتكلفة وجهدًا أقل. جهاز الاستشعار البيولوجي البصري هو جهاز يستخدم مجالًا ضوئيًا لاكتشاف وقياس الأنواع البيولوجية المختلفة مثل الحمض النووي والخلايا والبروتينات وأي عينات بيولوجية بدقة أكبر. كان الهدف من هذه الدراسة هو الكشف عن مستوى هرمونات الغدة الدرقية (تحفيز الغدة الدرقية (TSH) وثيروكسين (T4) وثلاثي يودوثيرونين (T3) وتركيزها من خلال استخدام اثنين من أجهزة الاستشعار الحيوية بالليزر بطريقة جديدة. تم جمع 45 عينة دم من المرضى الذكور والإناث وكذلك 15 من الأصحاء، تراوحت أعمارهم بين (20-50) سنة من المركز التخصصي لأمراض الغدد الصماء والسكري (SCED)، ولكل هرمون (15) عينة من المرضى و5 من الأصحاء، وعينة TSH مكونة (2 ذكور و 13) عينات المرضى و5 عينات من الأصحاء (4 أنثى و 1 ذكور)، T4 (3 ذكور و 12 أنثى) بينما الأصحاء (1 ذكور و 3 أنثى) عينة و T3 (4 ذكور و 11 أنثى) من لمرضى و(1 ذكور و 4 أنثى) من الأصحاء تم استخدام عينة مصل لقياس تركيز هرمونات (T3، T4، TSH) في هذا العمل، يتم استخدام إعداد سحب من المستشعرات الحيوية الضوئية للكشف عن تركيز هرمون الغدة الدرقية (مستشعر الألياف الضوئية أحادي الوضع (SMF1، SMF2) ومستشعر الألياف الضوئية متعدد الأوضاع (MMF1، MMF2)). تكون نتائج امتصاص ضوء الليزر بواسطة عينات عالية التركيز أعلى وتتناسب عكسيًا مع شدة الضوء، وهذا يعني أن شدة الضوء في جانب الكاشف كانت عالية عندما يكون تركيز الهرمونات منخفضًا. كان متوسط $\pm SD$ لكثافة المصل T4 بين (SMF1 و SMF2 و MMF1 و MMF2) بشكل كبير ($p \leq 0.05$) وكذلك متوسط $\pm SD$ لشدة TSH في المصل بين (SMF1 و SMF2 و MMF1 و MMF2) كان كبيرًا ($p \leq 0.01$) بينما كانت القيم المتوسطة $+ SD$ للمصل (T3) المقاس بين (SMF1 و SMF2 و MMF1 و MMF2) غير معنوية ($P = 0.210$) يمكن تفسير هذه الظاهرة على أنها ارتفاع امتصاص الضوء بواسطة العينات (هرمون TSH و T4 و T3) نتيجة اختيار الليزر المناسب الذي يعتمد على امتصاص العينات لطول موجة الليزر. يعتبر المستشعر الحيوي للألياف الضوئية متعدد الأوضاع لمستشعر واحد (MMF1) هو النوع الأكثر فعالية لأن إشارة

كثافة الألياف متعددة الأوضاع لها عدد كبير من الأوضاع مقارنة بالألياف أحادية الوضع (SMF1، SMF2) والألياف متعددة الأوضاع (MMF2) عند إنشاء نوعين من أجهزة الاستشعار الحيوية (أحادية الوضع ، متعددة الأوضاع (SMF1 ، SMF2 ، MMF1 و MMF2)) باستخدام ليزر ديود ذو ضوء أزرق (450 نانومتر) لقياس مستوى (TSH، T4 و T3) في عينات الدم ، تم مراعاة جهاز استشعار الليزر متعدد الأوضاع أفضل جهاز استشعار حيوي للكشف عن تركيز ثلاثة هرمونات في العينة بالإضافة إلى أنه حساس للغاية في نقل شدة الإشارة الضوئية. جهاز الاستشعار البيولوجي هو الأكثر دقة ، مع التشخيص السريع ، والطريقة الأقل تكلفة من الطريقة التقليدية لتجنب أي تغييرات بيولوجية في عينة الدم تؤدي إلى تغييرات في الخصائص البصرية (امتصاص) عينة الدم.



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المتحسس الحيوي اليفي البصري لكشف مستويات هرمون الغدة الدرقية

رسالة مقدمة الى
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المدرس الدكتور

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