Chapter-2

Literature Review

2.1 Introduction

To carry out the research, articles and patents were included that were published in between 1992-2018. The keywords which were used to find the relevant literature were: Drug delivery methods, Traditional and modern drug delivery methods, Open loop drug delivery, Closed loop drug delivery, CLAD (Closed Loop Anesthesia Drug Delivery), Automatic drug delivery, Computer controlled drug delivery, Pharmacokinetics, and pharmacodynamics in drug delivery, Role of IoT in healthcare, Patient monitoring, Telemonitoring, Expert System Facility in Healthcare and Clinical Decision Support System. The database used to find the literature was PubMed, Google Scholar, Web of Science and Ebscohost.

2.2 drug delivery

Traditional drug delivery (Paolino, Sinha, Fresta, & Ferrari, 2006; Hughes, 2009) methods include chewing leaves and roots of medical plants and inhalation of soot (Raskin et al., 2002), which are burning of medical substances. The major drawback of such kind of drug delivery system was the lack of uniformity. Which led to the new drug delivery methods like pills, capsules, syrups, tablets, etc. in the later part of the eighteenth and early nineteenth century (Paolino et al., 2006). Drug delivery with the invention of vaccines was possible with the invention of penicillin in late eighteen. To obtain the desired therapeutic effects, the appropriate amount of drug must be absorbed and conveyed to the site of action. The drug may be introduced through multiple routes such as oral, rectal, parenteral transmucosal, etc. Due to advancement in technology, it is quite possible to release controlled drug
delivery. A large number of approved devices have originated due to the origin of biotechnology (Patwardhan & Mashelkar, 2009; Hughes, 2009). To obtain the desired therapeutic effects, the appropriate amount of drug must be absorbed and conveyed to the site of action. Therefore, it is possible to deliver the drug at a specific rate for a defined period independent of the local environment. (Jain, 2008). Drug delivery is a process of administering the pharmaceutical compound in human beings to achieve therapeutic effects. Therefore, the rate and the amount of the drug must be calculated precisely as any mishandling can lead to certain complications in a patient. Delivery methods become important factors as they decide the vital target area. Therefore, doctors take a number of factors while choosing the best drug delivery system like symptoms, age, and weight of the patient, lifestyle and clinical conditions, etc. Although numerous drug delivery systems are available for treating disease, but proper dosing can be made more precise using pharmacokinetic and pharmacodynamics models (Bailey & Haddad, 2005).

2.3 Traditional and modern drug delivery systems

Patient safety relies on multiple parameters, where one of the significant issues is medication error (Chapuis et al., 2010). There are many reasons behind the occurrence of medication errors such as transcription, dispensing and administration stage of drug therapy (Chua et al., 2003). Dispensing medication is risky because such kinds of errors are increasing in community and hospital pharmacy across the world (James et al., 2009). In traditional manual drug delivery methods errors occurred due to lack of mathematical skills. Which may lead to underdosing or overdosing of drug (Haigh, 2002; Wheatly, R.G., Schug, S.A., Watson, 2001). Approximately 1200 people died in England in 2001 and Wales as a result of drug error which is a rise of 500% over the last decade (Scott, 2002). According to a study, adverse drug events
due to medication errors were found at a rate of 6.5 per 100 patients (Kaushal, Barker, & Bates, 2001). Therefore, it affects the patients in terms of an extended stay in the hospitals. A study was conducted in the Felege Hiwot Referral Hospital (inpatient department), where 82 nurses were involved in the research for the study. Authors had analyzed the data using SPSS, and it was found that dose errors were 23.1%, due to wrong calculation of the drug (Feleke, Mulatu, & Yesmaw, 2015). Manual drug delivery is a form of traditional drug delivery, where the drug is delivered through oral route or intravenous routes in the types of injections and drug is circulated through the blood circulation. Chances of medication errors in manual drug delivery systems are more comparable to computerized controlled drug delivery systems.

As chances of miscalculation in manual drug delivery system are more; so the critically ill patients admitted in the ICUs are susceptible to higher risks of the adverse effects of drugs (Chandramouli, 2018). Therefore, the chances of medication errors are more. Drug errors in case of pediatric patients are increasing due to wrong calculation of the drug because a drug is calculated based upon the weight of the patient (Murray, Streitz, Hilliard, & Maddry, 2019).

Such types of errors can be significantly reduced through computer systems because they help the doctors to make critical clinical decisions (Bates et al., 1998). Drug calculation errors with the computerized system are reduced by 40% (Murray et al., 2019). Some computer-based decision support systems are available that assist the healthcare professionals in making good decisions based upon a computer application (Kesselheim, Cresswell, Phansalkar, Bates, & Sheikh, 2011).

Due to advancement in technology, it is possible to deliver controlled drug using infusion pumps. Newly developed “smart intravenous infusion pumps”
have been designed to reduce the rates of these types of errors (Jacobi, 2016; Eskew, Jacobi, Buss, Warhurst, & Debord, 2002). It is possible to deliver drug effectively through infusion pumps in large or small quantity (Chandramouli, 2018). Such kind of infusion pumps have drug libraries and provide point-of-care decision support feedback for overly high or low intravenous infusion rates and doses (Rothschild et al., 2005).

Computer controlled drug delivery is a type of modern drug delivery, where the exact amount of drug can be delivered compared to manual DDS. Automatic drug delivery system using infusion pumps/ drug dispenser which comes with controllers to control hypnosis has improved tremendously in recent years. They can be further classified as semi-automated and fully automated DDS.

2.3.1 Semi automated DDS

These are the computer controlled system where doctors have to make manual adjustments while the infusion of the drug. Open loop drug delivery system is a semi automated DDS. Base upon their experience, the clinician sets the Target Concentration (TC) and let the system adjust the infusion rate automatically (Stephane Bibian et al., 2015). Drug delivery using open loop is time consuming and efficiency of the drug delivery entirely depends upon the expertise of the patient (Michel M.R.F. Struys et al., 2006). A continuous drug adjustment may put an extra work load on clinician, therefore, the chances of miscalculation is more (M. M R F Struys et al., 2002; Soltesz, Dumont, Van Heusden, Hagglund, & Ansermino, 2012).

An open loop system as shown in Figure 2.1 directly controls the output without getting any input from the doctor. Pre-programmed infusion pumps are used for this purpose which are predicted to have desired effects. This prediction depends on the prior information of the pharmacokinetics of the drug (Biebuyck et al., 1992). The major drawback of open loop drug delivery
systems is lack of feedback mechanism. As in case of physiological changes in patient, the doctor has to make manual adjustments. However, where self administration of a drug is required, it always delivered fix amount of drug. For example, many diabetic patients administer bolus of insulin, where changes of bolus must be according to the insulin requirements of the body. This will result in increased uptake into the muscle cells and decreased uptake into the liver relative to a healthy patient. Closed loop drug delivery is an alternate of open loop where the proper insulin dose is delivered after monitoring the glucose level in real time (Farmer Jr, Edgar, & Peppas, 2008).

Therefore, an open loop drug delivery system may release overdose or underdose (Hartlaub, Jerome T, and Bourget, 2004). In a study by (Yong et al., 2017), the total cost of anesthesia and anesthetic were calculated and it was found that the total cost of anesthesia in a closed loop is decreased. However, in other drugs like remifentanil no significant change was observed.

2.3.2 Fully Automated Drug Delivery System

Computer controlled drug delivery systems where least human intervention is required considered as fully automated DDS. Closed loop DDS is a form of
fully automated DDS. The best part of a closed-loop system is that they can make decisions at their own to maintain a defined target because they are computer programs designed to maintain a target effect (Michel M.R.F. Struys et al., 2006). Automation in the field of drug delivery helps the clinician to limit the effects of individual patient variability related to the quality of the drug, utilize the time for desirable clinical state and improve the safety measures to provide quality care (Stephane Bibian et al., 2015). Closed loop control offers several benefits over manual delivery to patients because of the frequent changes in the rate of drug delivery (Absalom, Anthony R and Sutcliffe, Nicholas and Kenny, 2002).

A closed-loop system as shown in Figure 2.2, senses the output, compares it with the set point and accordingly calculates the new rate of infusion. This kind of system is also known as a feedback control system (Biebuyck et al., 1992). The control variable in a closed-loop system must be measured carefully. Therefore, an ideal sensor should be chosen for effective dose response (Michel M.R.F. Struys et al., 2006). Closed loop drug delivery is effectively used by anesthetists to deliver an accurate amount of drug.

Figure 2.2 Feed - back Controlled Closed- Loop Drug Delivery System
Presently there is no standard to measure the depth of anesthesia; surrogate measures have to be applied as a controlled variable (Absalom, Anthony R and Sutcliffe, Nicholas and Kenny, 2002).

As the depth of hypnosis cannot directly measure, so anesthetist has to include surrogate measures. Through EEG several computerized univariant parameters can be extracted which helps to regulate the depth of hypnosis (M. M R F Struys et al., 2002). Traditional signs to measure the depth of anesthesia includes blood pressure, lacrimation, facial grimacing, movement or diaphoresis.

Due to the advancement in signal processing researchers can associate DOA (Depth of Anesthesia) through the features extracted from processed EEG (Huang, Lu, Nayak, & Roy, 1999). However, parameters like the Bispectral Index (BIS) and auditory evoked potential index (AEPEX) derived from EEG helped the clinician to measure the depth of anesthesia.

![BIS values to measure DoA](image)

Figure 2.3 BIS values to measure DoA
BIS provides a reliable and highly repeatable index of hypnosis. Therefore, it is used by anesthetist for closed-loop drug delivery as a feedback controller (Biebuyck et al., 1992). Bispectral Index (BIS) is used to measure depth of hypnosis as shown in Figure 2.4. BIS has an advantage over other electroencephalographic (EEG) variables. Closed-Loop Anaesthesia Delivery System (CLADS) used BIS as control variable.

The values shown in the Figure 2.3 are discussed in a study by Bibian et al. (S Bibian, Ries, Huzmeman, & Dumont, 2005). The BIS value lies in the range 0-100. A BIS value lies in the range 90-100 portrays the fully awake state, whereas values in the range of 60-70 and 40-60 represents light hypnosis and moderate hypnosis respectively (Michel M.R.F. Struys et al., 2006). When the closed-loop system is used for the administration of propofol (name of the drug for anesthesia) using bispectral index in cardiac surgery it was found that the closed-loop system proves better than the manual system. Table 2.1 shows that CLAD guided by BIS provided clinically adequate and satisfactory results than the manual system.

<table>
<thead>
<tr>
<th>Table 2.1 Anesthetics variables (mean ± SD)</th>
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<tr>
<td>Anaesthetic variables (mean ± SD).</td>
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<tr>
<td></td>
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<tr>
<td>CLADS (n = 19)</td>
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<tr>
<td>Manual (n = 18)</td>
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<tr>
<td>$P$-value</td>
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<td>--------------------------------------------</td>
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<tr>
<td>Induction time (s)</td>
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<tr>
<td>242 ± 55</td>
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<tr>
<td>160 ± 47.5</td>
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<tr>
<td>0.01*</td>
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<tr>
<td>Induction dose (mg/kg)</td>
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<tr>
<td>1.2 ± 0.3</td>
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<tr>
<td>1.7 ± 0.3</td>
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<tr>
<td>&lt;0.001*</td>
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<tr>
<td>Lowest BIS during induction</td>
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<tr>
<td>45 ± 5</td>
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<tr>
<td>38 ± 9</td>
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<tr>
<td>&lt;0.001*</td>
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<tr>
<td>Percentage fall in MAP from baseline after induction</td>
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<tr>
<td>23.8 ± 8.6</td>
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<tr>
<td>33.4 ± 11.3</td>
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<tr>
<td>0.004*</td>
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<tr>
<td>Total propofol (mg/kg)</td>
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<tr>
<td>13.3 ± 3.8</td>
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<tr>
<td>17.1 ± 6.9</td>
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<tr>
<td>0.041*</td>
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<tr>
<td>Total fentanyl (µg/kg)</td>
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<tr>
<td>10.5 ± 2.5</td>
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<tr>
<td>12.5 ± 3.2</td>
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<tr>
<td>0.046*</td>
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</table>

$P < 0.05$. CLADS, closed-loop anaesthesia delivery system; BIS, Bispectral index; MAP, mean arterial pressure.
According to reports from different research groups closed loop systems provide some distinct advantages over the standard clinical practice (Manberg, Vozella, & Kelley, 2008) and BIS-guided propofol administration (Biebuyck et al., 1992; Agarwal et al., 2009; Absalom, Anthony R and Sutcliffe, Nicholas and Kenny, 2002; Morley, A and Derrick, J and Mainland, P and Lee, BB and Short, 2000) proves that the closed-loop system is better.

![Diagram of DOH control system in closed-loop](image)

**Figure 2.4 DOH control system in closed-loop (Soltesz & Heusden, 2012)**

### 2.4 Pharmacokinetics and pharmacodynamics

Pharmacodynamics is the effect of a drug on the body whereas pharmacokinetic is effect of the body on a drug or it is an effect of an organism on the drug. So Pharmacokinetics is the study that demonstrates absorption, distribution, metabolism and excretion. To get the effective usage of any drug it is important to understand both pharmacodynamics and pharmacokinetics of a drug, also known as PK-PD model. In recent Target Controlled Infusion (TCI) pumps are developed by anaesthesiologists to control pharmacokinetics and pharmacodynamics (Stephane Bibian et al., 2015). Puri et al. evaluate pharmacokinetic for the Indian population.
undergoing surgery using propofol (drug) infusion (Puri & Dhawan, 2013). Study shows that the closed-loop drug delivery system controlled by pharmacodynamics feedback have benefit over open-loop (target controlled infusion (Agarwal et al., 2009).

Figure 2.5 Three-compartment model

K12 = rate constant from central to tissue compartment
K21 = rate constant from tissue to central compartment
K13 = rate constant from central to deep tissue compartment.
K31 = rate constant from deep tissue compartment to central compartment
K10 = Elimination constant

Figure 2.6 Three Compartment model with three volume of distribution
2.5 Telemonitoring

Due to advancement in information and communication technology all paper-based records are transforming into e-health records. The health monitoring system creates a network between patient and physician to access the required information from the e-health records. Based upon the collected information health monitoring system update the status of the patient to the doctor. Therefore, it helps to improve the life span of a patient (Ramu, 2016). Telemonitoring helps to monitor the patient at home from a remote location which helps to decrease the number of hospitalization (Trappenburg et al., 2008).

It shows a great potential to improve the health of patients suffering from diabetes and heart problems (Louis, Turner, Gretton, Baksh, & Cleland, 2003; A. Farmer, Gibson, Tarassenko, & Neil, 2005). According to a report given by the ICMR (Indian Council of Medical Research), it was estimated that 62.4 million people had diabetes in India. This percentage is increasing due to insufficient or lack of awareness, illiteracy, little access to health care due to problems in transportation, lack of professionals in diabetes.

Heart failure (HF) is the major reason for the hospitalization of elderly persons (KA, LC, Hudock, & Litman, 2008). Therefore, old age persons are readmitted within 3-6 months of discharge (Rich, 1999; Proctor, Enola K and Morrow-Howell, Nancy and Li, Hong and Dore, 2000). According to a study by (Ware, Seto, & Ross, 2018) home telemonitoring improves heart failure cases and using this technology patient can handle the schedule of visiting to the clinic. Authors have reviewed the heart failure outcome and impact of heart failure using home telemonitoring. It is also used effectively to control blood pressure. The blood pressure could be controlled even better by using telemonitoring (Parati, Dolan, McManus, & Omboni, 2018). The TASMINH4 investigators work on the efficacy of the self-monitoring of
blood pressure. The authors have executed the implementation over 1182 participates to measure their blood pressure, where all participate were asked to monitor their blood pressure by themselves (McManus et al., 2018). According to a study by (Losiouk et al., 2018), a telemonitoring service is developed for young patients affected by the type 1 diabetes in past few years. The paper has shared the method and results of implementing the experiment. The study also aimed to analyze the parents' perceived usefulness of the service.

In another study telemonitoring is used to reduce the rate of mortality for the patients, suffering from heart failure. The study showed a significant benefit of the telemonitoring when \( \geq 3 \) biological data are transmitted (Yun, Park, Park, Lee, & Park, 2018). Telemonitoring is a promising technology used in healthcare for improving heart failure outcomes (Chaudhry et al., 2010).

The screening or checking for diabetes is hardly done in a rural area which results in improper treatment. The research came up with a model of diabetes healthcare to care for patients more effectively and affordably using a mobile van having equipment for the treatment to diagnose and in the emergency case. The patients can contact to expert with the help of trained technicians utilizing satellite communication. In this paper, it was concluded that cost-effective healthcare can be achieved through the telemedicine (Mohan, V., & Pradeepa, 2014).

A study was conducted to examine the effects of home telemonitoring (TM) of patients with severe chronic obstructive pulmonary disease (COPD) (Shany et al., 2017). The paper has a description of implementing a randomized controlled 12-month trial of 42 patients with severe COPD. The result also suggests that TM had a reduction in COPD-related admissions, emergency department presentations, and hospital bed days. It provides a way to monitor a patient from a remote location.
This technology can also be applied to monitor the old age people to regularly monitor their health status, which may imply a reduction in their ability to live independently (Noury, Virone, Ye, Rialle, & Demongeot, 2003). Smart homes (Noury et al., 2003; T. G. Farmer et al., 2008) are developed to provide the complete health status of a patient. In recent years, microelectronic systems to enhance medication intake have been designed to enable monitoring of patient behaviour, which helps to decrease the rate of morbidity in patients. (Schmidt, Silke and Sheikzadeh, Sarah and Beil, Britta and Patten, 2008; Schneider, Marie-Paule and Stubi, 1998).

Telemonitoring was defined as the use of remote (Bluetooth-enabled) monitoring technology that collects information (blood pressure and weight), send information electronically to caregivers, and allows for caregiver-patient communication (Albert et al., 2017).

In another study the cost of the self-monitoring and telemonitoring are compared (Fasterholdt et al., 2018). Authors implemented an experiment with 374 patients to study either telemonitoring or self-monitoring. According to the study by authors telemonitoring was cost-effective than self-monitoring.
2.6 Internet of Things in Healthcare

Nowadays, the role of a computer network connects all the people through the internet with each other, in the similar way IoT makes it possible to connect all the objects. Ther term IoT is actually a network of objects communicating with each other. The use of Internet of Things (IoT) is playing a vital role in the field of health care. IoT enables sensors or devices or objects present in the network to communicate independently with other objects in the network. Therefore, every object can be considered as a smart object (Purri, Choudhury, Kashyap, & Kumar, 2017). It can send and receive data over the internet without human interference (Kaur & Jasuja, 2017).

In the current era, there is a deep connection between healthcare industries and technology. The scope of internet of things and big data are the areas where expansion is increasing drastically with the help of new opportunities. IoT can provide smart and innovative services such as ease of access to medical devices, continuous monitoring/care and quality of life (Alansari, Soomro, Belgaum, & Shamshirband, 2018).

In rural areas, there is a lack of medical facilities and it has been observed that doctors are there but they are not willing to give their services. According to a paper presented by (Singh, 2016) an IoT based solution is demonstrated using RFID to track and find the specialists. An android based application (ECG Android app) is developed by authors to monitor the ECG of the patient using an android phone (Mohammed et al., 2014).

Human beings are highly interested and started accepting wearable bio-sensors, many new assignments for particular e-Health and m-Health technologies have integrated (Firouzi et al., n.d.). Alansari et al. demonstrated the application of IoT in healthcare (Alansari et al., 2018), according to the authors the areas of IoT in healthcare are shown in table 2.2
Fall Detection | Helpful for the old age and physically challenges people.
---|---
Medical Fridges | To measure and inform the internal temperature so is to protect the organic elements.
Sportsmen Care | The application is specifically useful for the professional sportsmen to measure the physiological parameters such as weight and blood pressure etc.
Patient Surveillance | Specifically used for monitoring of the patient from the remote location.
Chronic Disease Management | Taking care of the patients suffering from chronic diseases in the absence of attendant. Therefore, it is helpful to reduce number of attendants in the hospitals.
Ultraviolet Radiation | Is helpful to notify people not to enter in an ultraviolet area.
Sleep Control | Helping to capture the data of a patient during the sleep hours.
Dental Health | Enables dentist to know the brushing habits of a person through a smart toothbrush.

The technology like WSN (Wireless Sensor Area Network) enables to sense, monitor and to track the data using intelligent sensors. The advancement in this technology contributes to the development of the IoT (Da Xu, He, & Li, 2014).

WSN is a cost-effective ad hoc network which provides various services to monitor and control the healthcare, home, industry and military (Catarinucci et al., 2015). In another work, WSN technology is used for pervasive healthcare applications. The technology is providing monitoring and tracking.
services inside an educational institute (Redondi, Chirico, Borsani, Cesana, & Tagliasacchi, 2013).

Kalarthi, 2016 defines the architectural view of a smart health care system which was targeted to provide quality health care using IoT. With the help of this model body parameter of patients' can be transmitted in real time. Sensors are attached with the patient to collect the body parameters of the patient and the received data were transferred to the controller (Arduino Uno) and transferred to the cloud.

The information gathered was stored in the MySQL database. The database manages the data and also provides access to that data. An Android application was developed to view the patient’s data (Kalarthi, 2016). Bui and Zorzi, 2011 focused on the use of IoT for e-Health communication and to secure the precious life of patients through low cost and low power devices. Patient-related information is sent via the WBAN (Wireless Body Area Network) to HCR (Health Care Record) database (Bui & Zorzi, 2011). In another study remote web-based ECG monitoring system is proposed.
Mishra, Kumari, Sajit, & Pandey, 2018). Authors had used ECG sensor (AD8232) by Texas Instruments to transmit the data at remote location. The collected data is transmitted to MQTT cloud which can be accessed by the web application.

Remote monitoring of patient(s), including vital signs, audio and video is becoming a necessity, especially when a patient is in transits. By transmitting the vital parameters of the patient to a doctor reduces the time for initiating treatment and allows the emergency crew to be better prepared (Meystre, 2005). Similarly, smart beds have been implemented by some hospitals to detect the movement of the patient, i.e. when a patient attempt to get up. These smart beds can also self-adjust without the intervention of the nursing staff (Laplante, Kassab, Laplante, & Voas, 2018).

In recent years, there had been increased research in ICT (Information and Communication Technology), particularly in the area of Wireless sensors network technology, low power microcontroller may create the very backbone of such a remote healthcare system which enables delivering high-quality resource-optimal care “anytime anywhere” (Maharatna, Mazomenos, Morgan, & Bonfiglio, 2012).

An IoT based solution is developed by (Purri et al., 2017) to transmit the heart rate and body temperature of a patient using sensors to the mobile phone of the specialist. The heart rate sensor is attached with the Xbee transmitter, which transmits the data to raspberry pi using Xbee receiver. Raspberry Pi is transmitting the data to the cloud which can be viewed by the doctor through the mobile phone. Therefore, the technology is removing the gap between the doctor and patient. Now a doctor can view the patient's physiological data even from the remote location.

The telecommunication system is also playing a significant role in this process, it is quite possible to deliver audio, video and text data due to the high-speed data rate. Mohammed et al. developed ECG waves monitoring for the Android platform. IOIO-OTG board is used, which can communicate with
Android devices to transfer sensor data through Bluetooth connection (Mohammed et al., 2014).

Figure 2.9 The vision of IoT by Jon Berkley (PANG, 2013)

Bingchuan et al. proposed web-based real-time monitoring system, CARA (Context-Aware Real-Time Assistant) that may be used to analyze real-time vital parameters of a patients and home monitoring system for self-governance for elderly persons (Yuan & Herbert, 2011).

Shaosheng Dai et al. recommended the prototype of a wireless physiological multi-parameter monitoring system which was supported on mobile communication (Dai, Shaosheng and Zhang, 2006). This system facilitated a patient to monitor his/her physiological parameters, along with parameters were uploaded in a central management system of hospitals. The technology
facilitated a doctor to make a diagnostic conclusion. Remote monitoring of vital signs for CHF (Chronic Heart Failure) patients enables the medical staff to diagnose the patient without regularly visiting a patient and take appropriate action (Saponara et al., 2012). Electronic monitoring devices such as E-Stethoscope, Blood Pressure monitor, Pulse oximeter, Glucometer, Electrocardiograph, etc. were used for distance monitoring of the patient (Balas & Iakovidis, 1999).

The key element of the presently developed remote health monitoring systems is to transmit the vital parameters of the patient to a remote location. Thanks to growth in the technology especially in Wireless Sensor Network (WSN) that allow transmitting vital parameters of the patient.

Recent technological advancement in the field of sensor area network allows the researchers to transmit the physiological data of the patient to a doctor at a remote location. Therefore many patients can be benefited from continuous monitoring (Jovanov, Milenkovic, Otto, & De Groen, 2005). Wearable sensor can be used for continuous health monitoring in ambulatory settings (Jovanov et al., 2005). On the other hand, there are some security issues, which are associated with this technology. When patient data are transmitting to a remote location it must be secure, safe and reliable (Witting, 2006).
2.7 Expert System facility

Expert system plays an important role to improve quality of healthcare. A rule-based system was developed to diagnose patients suffering from cardiac problems. This system worked on some pre-defined rules to generate alarms. The alarms were generated based upon a pre-defined threshold value. An intelligent telecardiology system was developed (Lin et al., 2010) which generates warnings in case of unstable ECG. These alarms can be transmitted on the phone of both doctor and patient.

Some case-based approaches had been developed to diagnose the patients having similar attributes (Heindl et al., 1997; Schmidt, R., Pollwein, B., Filipovici, L. and Gierl, 1995; Schmidt, Heindl, Pollwein, & Gierl, 1997). Many expert systems have been developed to assists healthcare professionals.

An expert system to diagnose the nausea and vomiting among the children had been developed. In comparison to the traditional approaches, this model worked accurately (Abu Naser & El-Najjar, 2016). The primary reason in the increasing rate of death is inaccurate identification of a disease. In a country like India there is a lack of specialized doctors, especially in rural areas; therefore, a clinical decision support system (CDSS) could be helpful to diagnose the diseases.

In another research a study was conducted to develop a clinical decision support system to classify and grade the retinal image was focused (Kumar, 2014). Eye disease like diabetic retinopathy causes problems in vision. The automatic CDSS using rule-based algorithm to classify the diabetic retinopathy as normal or abnormal had been developed and presented in the study.

CDSS is proposed to help healthcare professionals to take diagnostic decisions. The characteristics of a patient are matched through a knowledge
base system, subsequently this system generates specific recommendations (Garg et al., 2005). The literature related to CDSS depicts that it has the potential to improve clinical performances (Kaplan, 2001). A CDSS comprises of three important parts as depicted in Figure 2.11.

- Inference Engine
- Knowledge base
- User Interface

![Figure 2.11 Expert System Structure](image)

A smart CDSS to predicts diabetes disease is proposed (Lakshmi, Ahmed, & Siva Kumar, 2018) by using Decision Tree and K-Nearest Neighbor (knn) algorithms. A diagnosis expert system (DExS) for the diagnosis of human diseases at an early stage was proposed by authors which helped to treat the patients. The DexS respond based upon the patient's response.

Clearly, there is a need to enhance diagnostic techniques in order to reduce the number of unnecessary hospital admissions and to reduce the number of patients who are misdiagnosed and inappropriately discharged (Kong et al., 2012). Apart from the expert system data mining is also used effectively for the analysis of the data (Koh, Hian Chye, 2011). Both expert system and data mining techniques are used to improve health care.
2.8 Problem Statement

1. Traditional drug delivery systems were manual, where human intervention was more, therefore chances of medication errors were more (Chapuis et al., 2010; Haigh, 2002; Wheatly, R.G., Schug, S.A., Watson, 2001).

2. Computer controlled drug delivery systems with feed-back mechanism show tremendous improvement (Absalom, Sutcliffe, & Kenny, 2002; Stephane Bibian et al., 2015).

3. Tele-monitoring shows a great potential to improve the health of a patient (Louis et al., 2003; A. Farmer et al., 2005).

4. There is a need to enhance diagnostic techniques in order to reduce the number of unnecessary hospital admissions and to reduce the number of patients who are mis-diagnosed and inappropriately discharged (Kong et al., 2012).

2.9 Objectives

- To explore various types of Drug Delivery System and make the comparative analysis
- To design and develop the architecture of Dynamic Drug Delivery interface system that will be able to deliver accurately calculated drug(s) as per the vital sign based interface system with least human intervention by using hybrid technique.
- Merging of expert system facility and analyzer database within dynamic drug delivery interface for future reference.
2.10 Chapter Summary

This chapter is primarily focused on literature study of the drug delivery system, types and challenges of traditional and modern drug delivery system. It was found from the literature review that patient safety is a serious global threat in the healthcare, as a significant number of patients are harmed during healthcare. Major causes of the medical errors were wrong drug dosage, overdose, and underdose. It was also found that medication errors are increasing due to negligence, lack of mathematical skills and manual calculations of the drug by the nursing staff. Computer controlled drug delivery system such as open loop and closed loop overcome the risks associated with the manual drug delivery systems. Although in most of the studies open and closed loop system are used independently. The effect of a drug on the body and the effect of body on the drug is covered through the pharmacokinetics and pharmacodynamic models.

The literature review also depicts that the number of hospitalizations is also increasing. Therefore, technology like telemonitoring helps to decrease the amount of hospitalization. It shows great potential to improve the health of a patient.

The role of IoT is also playing a vital role in the field of healthcare. This technology allows sending the data of sensors over the network. Therefore, all the physiological data of a patient can be transmitted to the cloud, which may be accessed by the doctors from the remote location. The literature shows that many patients are taking benefit from the IoT in healthcare.