

Pharmaceutical Applications of Radio-Frequency Identification

Rohit Kalra, Pallavi Shetty, Srinivas Mutalik, Usha Y. Nayak, M. Sreenivasa Reddy, Udupa N.

Department of Pharmaceutics, Manipal College of Pharmaceutical Sciences, Manipal University, Manipal, Karnataka, India

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ABSTRACT

Radio-frequency identification (RFID) is a small electronic device that utilizes the radio waves for the purpose of security, personnel identification, surveillance, medical identification, patient history, library automation, baggage application, toll collection, file tracking, electronic payment, etc. Three types of RFID tags namely, active, passive, and semi-passive RFID tags, are currently available. The basic components of RFID system are RFID transponder, antenna, and transceiver. This review mainly focuses on the various applications of RFIDs in the pharmaceutical sector. RFID has potential applicability in pharmaceutical and healthcare sectors such as product tracking and inventory control, limiting the Bullwhip effect, supply chain management, maintenance of dyes and punches, preclinical study, identification of patients and hospital staff, avoidance of medication errors, etc., which have been discussed in detail. Besides having innumerable applications, RFID technology is in its early stages in pharmaceutical systems and hence its potential is required to be explored more in practical. The RFID systems are expensive which makes the adaptability of this system very difficult. Hence the development of low cost RFIDs is a big challenge at present and more research activities are required in this direction.


Introduction

Radio-frequency identification or RFID (pronounced as separate letters) is a general term that refers to a small electronic device which contains a small chip and an antenna that enables wireless transmission of identity.^[1] It refers to the application of RFID tag using radio waves applied to or incorporated into a product for the purpose of security, personnel identification, surveillance, medical identification, patient history, etc. RFID is an automatic technology that utilizes the radio frequency waves to transmit data between a reader and a RFID tag to identify, track, or locate that item.^[2] RFID device provides a unique identification of an object and is a contactless smart card which does not require physical contact between the scanner and the tagged item.^[3] RFID tags, depending on the transmitter and reader, can be utilized to scan and read up to a long distance (e.g., Smart Label RFIDs).^[4] It can be either implanted or used as a wristband which stores medical data of the patient.

RFID tags may be so tiny that consumers cannot clearly see them.^[5] RFID's capability to distinctively recognize each object, and firmly capture information without line-of-sight has many benefits in the pharmaceutical industry including insight, visibility and efficiency, accountability and brand protection, product safety, recalls and regulatory requirements, reducing theft and counterfeiting, etc.^[6] There are few recent articles on the applications of RFIDs in health system and biomedical fields.^[7-12] In this review, we discuss the various applications of RFIDs both in pharmaceutical and health care systems.

Comparison between radio-frequency identification and barcode

Both Radio-frequency identification (RFID) tags and barcodes provide information about the products. However, there are many differences between RFID tags and barcodes. Barcode readers require a direct line of sight as an electronic handshake to the barcode.^[13] Due to this, barcodes must be exposed outside the product, where it is subjected to greater wear and tear; whereas, RFID readers do not require a direct line of sight as an electronic handshake. The barcode range is much less; but RFID tags can be read from long distances. A barcode scanner can be pointed at a specific item and can read only that item; while RFID scanners basically create a sphere of activity within which they read all tags. Generally RFID tags have much faster read rates than barcode readers. Electronic components of RFID can be covered in a plastic wrap and hence they are more rugged than barcodes. RFID tags can also be set in the product itself, providing better ruggedness and reusability. Barcodes have no read/write ability; however, RFID

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Correspondence:

Dr. Srinivas Mutalik; E-mail: ssmutalik@yahoo.com

tags can be read/write devices. However, barcodes are commonly accepted because they are very economical and there are well-known standards for their application.^[14]

Types of RFID

There are three types of RFID tags: active RFID tags, passive RFID tags, and semi-passive RFID tags.^[15,16] However depending on the modes of storage of data, RFID tags can be of three types: read-write, read-only, and WORM (write once read many). In read-write type, the data can be added or overwritten. In read-only tags, the data can be stored at the time of make and later the data cannot be added or overwritten. In the WORM type, the data can be added once and overwriting is not possible later.^[17]

Active RFID tags

This type of tag is more sophisticated. Active RFID tags are larger and costlier to produce since they require a power source. These possess an internal battery, which is used to run the microchip's circuitry and to transmit a signal to the reader. Active tags have a stronger signal and are more reliable than passive tags as they can conduct a "session" with a RFID reader. They operate generally at higher frequencies like 455–950 MHz or 2.45–5.8 GHz. The signals are captured by the reader over a longer distance.^[18] Because of onboard power supply, the active RFID tags transmit the signals at higher power levels than the passive tags due to which they are more effective in "RF challenged" conditions.^[19] Practical ranges for the active RFID tags are hundreds of meters. They have an extended memory and a battery life of up to 10 years.^[14]

Following are the potential applications of the active tags:

- (i) in tracking containers and trailers during transportation
- (ii) in locating the people or things (in conjunction with GPS or GSM)
- (iii) to locate the personnel, with Bluetooth application, in the premises (e.g., locating doctors in the hospitals)
- (iv) in animal tracking
- (v) in security ID cards

Passive RFID tags

Internal power supply is not included within the passive RFID tags and hence they depend only on the RFID reader to transmit data. They are also known as 'pure passive', 'reflective', or 'beam-powered' tags. The reader supplies the electromagnetic waves to produce a current in the antenna of the tags. Then, the tag reflects the RF signal and produces information by modulating the reflected signal to the reader. In most passive tags, a small electric current produced in the antenna by radio frequency signal provides power for the complementary metal oxide semiconductor (CMOS) integrated circuit to transmit data. They operate comparatively at lower frequencies like 30–134 KHz or 13.6 MHz with a lower capturing range.^[20] Due to lack of onboard power supply, RFID tags are quite smaller so that they can be embedded in a sticker or under the skin, and are generally used for relatively short distances.

The major advantage of passive tags is that they operate without a battery and hence they are much less expensive and much smaller in size than active RFID tags. The disadvantages include: the short distance for reading the tag and requirement of a higher-powered reader than active RFID tags. These tags have been found useful in (i) apparel,

consumer goods, and asset tracking; (ii) ticketing; (iii) identification of vehicles; (iv) ID badges and access control; (v) entry pass, toll pass, and electronic toll collection; (vi) in transport/travel (buses, ferries, trains, and subway); (vii) tracking of books in libraries, etc.

Semi-passive RFID tags

Semi-passive RFID tags are identical to active the RFID tags as they also have an inbuilt power supply; but semi-passive tags do not transmit a signal until the RFID reader transmits the signal first.^[21]

Basic components of RFID and their working

Different components of RFID and their working are shown in Figure 1. A brief description of each component is given below.

- RFID tag (transponder) is programmed with unique information by electronic means and it has to be read by an antenna. Every RFID tag ("Smart Label") could contain 96-bits of information and a 40-bits serial number.^[16]
- An antenna attached to a microchip which emits the radio signals to activate the tag and to read and write the data. This assembly is usually enclosed within a protective layer which is determined by the type of application.
- A transceiver with decoder is used to retrieve the data stored on the RFID tag. This decoder decodes the data encoded in the IC of tags. These data are then passed to the host computer for processing.

Pharmaceutical and health care applications of RFIDs

Various applications of RFIDs include library automation, security and control applications, patrolling log applications, baggage application, file tracking, electronic payment, toll collection, etc.^[16] Different applications of RFIDs in the pharmaceutical and health care systems are shown in Figure 2 and some of the specific applications along with appropriate references^[22,23] are given in Table 1.

Product tracking and inventory control

RFIDs provide facility to the organizations to recognize and control their assets. RFIDs have a wide range of applications in product

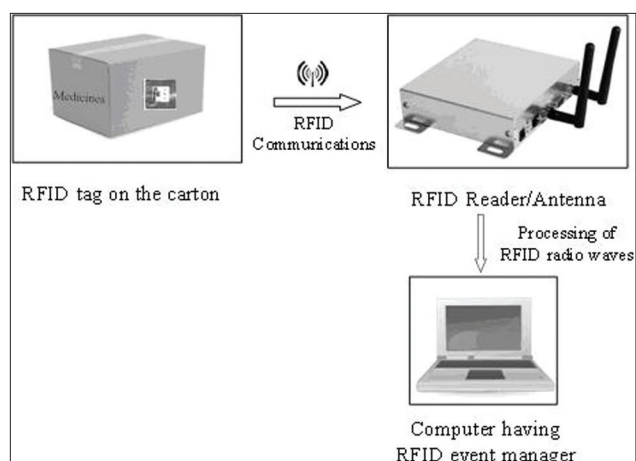


Figure 1: Working of different components of RFID

tracking, starting from the production of the goods in the plant to post-sales of the goods. The mobilization of pharmaceutical products may be regulated by RFID access control.^[24] RFID tags can be applied on the (i) assets which are frequently lost or stolen and (ii) the products which are underutilized or difficult to locate. They can also be applied to the assets which are under maintenance. RFIDs also ensure the expiration dates and improve expiration management. It lessens the time spent in the recognition of products considered for recall. WYZE-SCAN is one such asset management system that is beneficial in reducing labor costs and inventory inaccuracies, and also in monitoring inventory product life.^[25] The drug distributors can get an idea about the availability of drugs in their stores with the help of RFID systems, and hence they can have stocks of important drugs for emergency situations. If any person steals the product and leaves the manufacturing unit, then stolen goods could be traced even from outside the manufacturing unit.^[26] To avoid the removal of RFID tags from the products, they can be made very small or invisible so that the tags cannot be easily

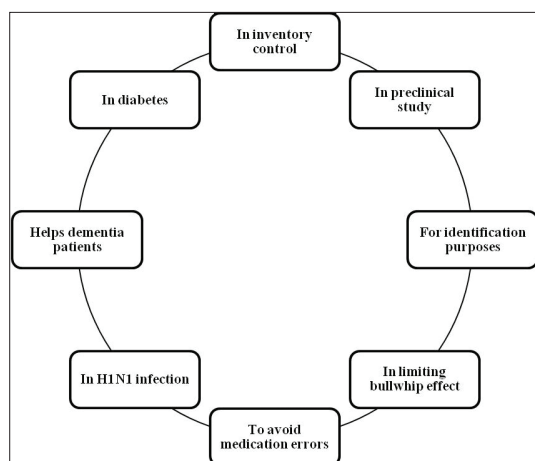


Figure 2: Different applications of RFIDs in the pharmaceutical and health care sector

Table 1: Some of the specific pharmaceutical and health care applications of RFIDs

Applications of RFIDs	References
Improving the communications between nurse and patient	22
Potential use of RFID technology in blood centres	23
Radio frequency identification devices in magnetic resonance imaging and computed tomography	63
Tracking of blood products to achieve higher productivity and safety in the transfusion medicine supply chain	64
Enhancement of inpatient medication safety	45
Intelligent Medicine Case System (iMec System) for assisting caretakers in medication monitoring	65
Helping the blind and visually impaired to easily navigate to their destinations in a public building	66
RFID based Medication Adherence Intelligence System (RMAIS) enables patient to take right amounts of multiple daily dosages at the right time	67
RFID based Smart Stretcher designed to constantly monitor the vital signs of the patient and to detect apnea during transfers within a hospital	68
RFID chips reduce the specimen labeling errors in surgical pathology	69
RFID tag can be inserted into dentures to facilitate the identification of decomposed bodies	70
RFIDs alleviate the scope of the counterfeit drugs	71

removed. Wi-Fi-based RFIDs can be installed to track the location of emergency equipment in some of the hospitals.^[27]

During transport, if the perishable products are not handled properly they get spoiled. In such cases, the hospitals have to maintain perishable inventory control to prevent additional cost of replacement and also to retain the goodwill of consumers. By using RFID technology for product identification, it is easier to assure the quality of moving objects. The RFID system assists to follow well-defined issuing policies for the products depending on the requirements; for example, first-in-first-out (FIFO) policy for vegetables, bread and last-in-first-out (LIFO) policy for blood products.^[28]

RFIDs in limiting the bullwhip effect

Lee *et al.* popularized the term “Bullwhip Effect,” where a retailer’s orders to their suppliers tend to have a larger variance than the consumer demand that triggered the orders.^[29,30] Because of tracking restrictions of conventional systems, it may not be possible to get precise information on the actual sales, which deepens the magnitude of the bullwhip effect. RFID systems may be used to collect the information and thus accurate and real time information on sales can be obtained. This will help to reduce the overall bullwhip effect.^[29] Reducing the bullwhip effect may be beneficial to industries where occurrences of supply-demand imbalances have high cost affairs.

Maintenance of dies and punches

RFID technology is used to automatically track the tools of the machines. The classical example in the pharmaceutical production field is tracking of dies and punches in the solid dosage form manufacturing units using RFID. The RFID tag permits a system to validate that the proper die/punch combination is installed or not. Replacing or servicing a worn die before it produces an inferior quality product or causes damage to the press is another potential application of RFID in the tableting section.^[31] These types of applications are comparatively easier to put into operation.

Counterfeit drugs

Pharmaceutical products are the main target of counterfeit. RFID is being considered as an important tool to fight against counterfeit drugs. A detailed outline how the counterfeit drugs can be prevented is given in Figure 3. RFID is known for its wonderful ability to uniquely identify each item. A large proportion of drugs in the international supply chain may be subjected to counterfeit.^[24] Sales of counterfeit drugs are predicted to explode if it is not dealt with effectively and rapidly. RFIDs have ability to document the sale and transfer of a drug through every step of the supply chain, from the manufacturer to the retail outlet. Popular drug products such as OxyContin^[32] and Viagra^[33] which are particular targets of counterfeiters have mandated the use of RFID technology. A well-known pharmaceutical company, Pfizer, has turned to RFID to overcome the counterfeit. In Pfizer’s RFID enactment, the tags are placed on drug packages (<http://www.rfidblog.org/entry/pfizer-introduces-rfid-authentication-system-to-fight-counterfeit-viagra/>). The authenticity of the product can be verified by scanning the RFID serial number of a particular package and confirming its authenticity with Pfizer directly, using their personal authentication

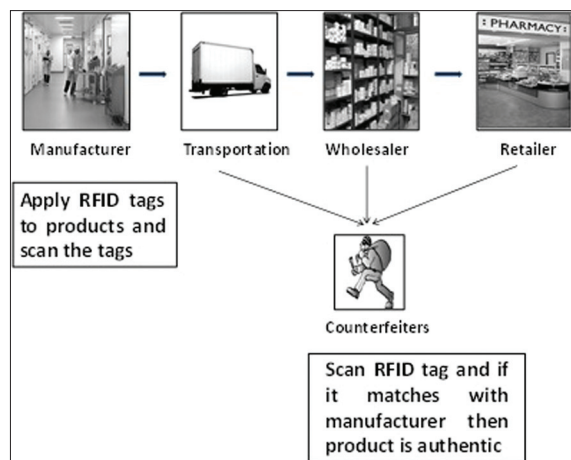


Figure 3: Prevention of counterfeit drugs using RFID systems

account on Pfizer's web site (<http://www.rfidjournal.com/article/articleview/2075/1/1/>)

GENTAG (Europe) has developed a simple and cost-effective wireless RFID tag to overcome counterfeit drugs (<http://electronicsbus.com/counterfeit-drug-detector-system-wireless-pharmaceutical-rfid-tags/>). It is molded inside the caps of the pharmaceutical packages. The consumer can check the authenticity of product through their cell phones before purchasing the product. GENTAG has patented RFID based skin patches for glucose monitoring, cardiac monitoring and for monitoring the UV radiation (<http://smartideabox.com/blog/gentag-rfid-diagnostic-skin-patch-technology-to-facilitate-processes-efficiency-in-healthcare/>).

Use of RFIDs in preclinical study

One of the important applications of RFID technology is "tagging the animals" [Figure 4]. RFID has become essential means in identification of animals after the epidemic Mad Cow Disease.^[34] RFID tags can be implanted for animal identification. RFIDs can also be used to tag the large number of animals used for the toxicity studies. Active RFID tags can also work as economical remote sensors that transmit telemetry (a technique which allows remote measurement and reporting of information) back to a base station.^[35]

Wireless medical telemetry services (WMTS) is the remote monitoring system used to observe physiological parameters of a patient (heart rate, blood pressure, and respiration rate) or behaviors of animals with the help RFIDs.^[36]

Identification of patients and hospital staff

RFID systems help the hospitals to recognize or to organize patients and authorize a particular staff to access the medical records.^[37] The implementation of RFID systems in the hospitals will allow observing the activities of the staff of the hospital.^[38] To have the advantages from RFIDs in hospitals, the patients may receive RFID wristbands or implants. The data of the patient's health or medical history can be maintained on a database automatically by the RFID tags. RFID chip implanted in a particular person would be extremely useful for the doctors if the person is brought into a hospital under serious conditions to know the patient's medical history, just by using a scanner that recognizes the RFID chip. These chips are very small in size (like grains of wheat or rice).^[39]



Figure 4: Tagging the animals with RFID chips (rabbits: on the ear; rats: in the neck)

The RFID tags can also provide the information about the health status of the patients by recording the blood pressures and heart rates.^[40] Placing the near-field communication (NFC) based RFID tags on the bracelets of infants has facilitated the doctors to track and treat the infants having pneumonia.^[40] Handwritten paper medical records are associated with many problems such as misreading and getting damaged or lost. On the contrary, RFIDs provide the digital record of the medical and treatment data by eliminating the problems of paper medical records. RFID tags when used as wristbands help to easily locate the disoriented patients and the high-risk patients. Other important uses of RFID chips in the hospitals may be the prevention of mother-baby mismatch, auto rejection of wrong parts, etc.^[41]

RFIDs for medical devices

It is obligatory to sterilize medical equipment before reusing them. RFIDs can be used to ensure whether the medical devices are sterilized. To achieve this, the devices can be provided with RFID tags. The RFID readers can be installed at the entrance to provide the status of such devices. The RFID tags help to save time by giving information on the exact location of the medical devices inside the rooms or chambers. Automatic heating devices that have a portable induction heater can also be controlled by RFIDs.^[42]

Prevention of mix-up between sperm and ova

To prevent the mix-up between sperm and ova, the Human Fertilization and Embryology Authority (HFEA) is considering labeling the containers of sperm and ova with RFID tags. An alarming sound would be produced if the wrong eggs and sperm containers are brought close to one another.^[43,44]

Avoidance of medication errors

Patient safety is a big challenge in health care systems. RFID based "Bedside Medication Verification System" has been used in some hospitals to improve the safety of the patients. Before administering any drugs, nurses use a portable RFID reader to ensure the identification of the patients and medications. The RFID technology that provides identification, tracking, location, security, and other capabilities has been proven as an efficient and safe way to manage the operational processes.^[45] RFID tags are also useful for locating and tracking the activities of the neonates.^[46] With respect to most of the pharmaceutical products, it is mandate for the companies to conduct exhaustive clinical trials before launching new products in the market. The RFID technology aids the tracking

of drug usage in clinical trials. It also eases the process of data collection in the clinical trials.

RFIDs in contagious diseases

Another application of using RFIDs is the prevention of the healthy population from the infectious disease such as H1N1, SARS, or tuberculosis.^[47] As per WHO, H1N1, a widespread epidemic disease, caused nearly 8000 death till November, 2009.^[48] RFIDs can play an important role to prevent the spread of pandemics. It can trace the records of contact between the patients and the hospital staff. The hospital would also provide RFID wrist-bands to the patients to strictly control the movements for safety. Through the application of RFID readers, the system will track all the follow-up movements of the patients. It therefore strengthens the safety and efficiency between the patients in the interest of public health.

RFIDs in dementia

RFID-based Health Research Management and Evaluation System (HERMES) can be set up to watch the movements of the patient. Based on the information collected, it may be used for diagnosing dementia at early stages. RFID has already been employed to look-after the dementia patients at medical care facilities, but it would be used to diagnose this disease at onset. A computer program is used for scanning patterns of movement of the person and the RFID system generates the data which are then incorporated into the program to analyze the data in a scientific manner. Early diagnosis of this disease becomes more vital as some drugs would not work if the patient takes them after the brain reaches a certain stage of decaying.^[49] Many patients with dementia become disoriented and try to escape the territory. This tendency to flee becomes a major threat to the health and safety of the sick residents. These patients may be outfitted with RFID tags that activate alarm sound if they approach boundaries or exits.^[50]

RFIDs in lumpectomy

Usually for breast cancer patients, both radiological and surgical procedures are scheduled on the same day. The general procedure in locating the tumor is by inserting a wire into the lesion to mark the tumor location. Then ultrasound, stereotactic, or mammographic guidance is used to identify the exact location of the tumor mass. To make this procedure easier, SenoRx, a USA-based company (www.senorx.com) has provided RFID-based equipment to diagnose and to treat breast cancer. This equipment offers the radiologists a new technique for marking the location of a tumor before surgery.^[51] SenoRx Inc. states that this equipment decreases the risk of infection, which is due to wire insertion and helps the surgeons to locate the exact position of tumor mass.

Prediction of ovulation cycles

In the ovulation cycle, generally there will be an increase in body temperature up to 1°F after the ovulation stage. This minute change in temperature cannot be detected by conventional thermometers. Therefore, a specialized thermometer to track this little change in body temperature is required for women who are trying for pregnancy.^[52] Women must regularly check their body temperature

to know ovulation. Cambridge Temperature Concepts, UK, has designed a RFID-based system to help the women to better track little changes in the body temperature and predict ovulation cycles.^[53] The product called Duo Fertility is already available in the European market (www.duofertility.com).

RFIDs in cardiovascular disease

Many deaths may be due to unavailability of medical assistance or treatment in the emergency situations especially with cardiac and/or respiratory system failures. The most crucial seconds are those in which a person oscillates between life and death. RFIDs are being tried to provide in-time treatment in emergency situations to the patients. Passive RFID tags are used to capture and transmit a patient's medical data such as body temperature, pulse rate, or respiration rate to an integrated ground station. In the meantime, the antenna in the ground station can also obtain information regarding the position of the individual from the Global Positioning System. Data of medical information and location will save the lives by examining the medical conditions of at-risk patients and then by providing treatment in-time.^[54]

RFIDs in diabetes mellitus

Diabetic patients can control their blood sugar levels more precisely with the help of RFID system. A prototype medical device, which consists of a glucometer and an insulin pump, has been developed by Cambridge Consultants in conjunction with Philips Semiconductors.^[55] The glucometer and insulin pump are wirelessly linked together using the NFC.^[56] The operation of NFC glucometer is shown in Figure 5. The biosensor chip has a glucose sensor, a passive RFID tag, and an integrated circuit. A wireless scanner reads and displays the glucose level. After recording the blood-sugar reading, the device will suggest a bolus dose of insulin, if glucometer indicates a high blood sugar level.^[57]

RFIDs in supply chain management

Present studies regarding RFID in supply chain management are concentrating on transportation management, inventory management and logistics, warehouse management, production scheduling, order management, asset tracking and object location, etc.^[58,59] RFID tags have the potential to perform rapid scanning of multiple packages without direct physical contact. This extremely reduces the time required to track individual assets

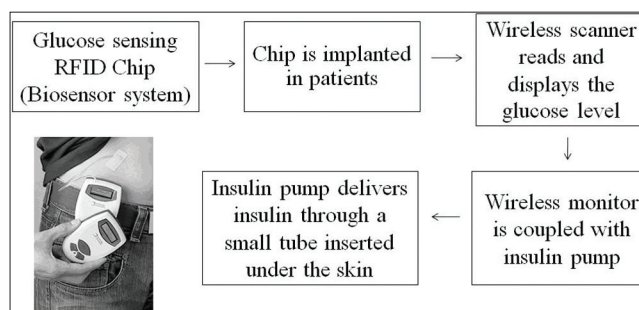


Figure 5: Flow-sheet showing the working of a NFC glucometer (the figure of NFC glucometer within the flow-sheet is produced from www.cambridgeconsultants.com/news_pr175.html with permission)

through supply chains. RFID technology can be used to automate different steps in the supply chain—from the simple tasks (such as moving goods through loading docks) to the complex tasks (such as collection and management of huge information/data on the goods in very little time). Because of the development of standards, most organizations are intending to track shipments among supply chain partners. Tracking of goods is considered as a good prospect to provide an efficient visibility of inventory which makes it easier and faster to handle the transaction of goods. RFID can improve the traceability and visibility of products throughout the supply chain, and can accelerate the processes such as tracking, checkout, shipping, and counting.^[60,61] RFID technology improves the productivity and quality of supply chain by reducing costs (such as labor costs), inventory levels, lead times, and stock outs; increasing manufacturing flexibility, inventory visibility, inventory record and order accuracy, and customer service.^[24] It has been reported that after implementation of RFID technologies, Procter and Gamble and Wal-Mart simultaneously reduced inventory levels by 70% and improved service levels from 96% to 99%. Additionally, by rearranging the supply chains, they also reduced the administration costs.^[62]

Conclusions

RFID technology is in its early stages and hence its potential in the pharmaceutical sector is required to be explored. By means of RFID technology, some industries have increased their efficiency and there is no exception for pharmaceutical and health care organizations. Few hospitals are already using this technology successfully to provide better health care to the public. Specifically RFID technology is being used in hospitals to keep real-time track of the location of patients, doctors, and nurses. Application of this technology in many pharmaceutical industries for various purposes has proven advantageous, as outlined in this review. However, the cost involved with this system is becoming a big constraint to apply RFID technology in all the possible systems or products. Hence, RFID would increase the cost of the treatment, finally leading to the financial burden to the patients. It has been considered that barcodes are more economical compared to RFIDs, although they are less advantageous. Hence, development of more efficient barcodes and low-cost RFIDs is a big challenge in the present situation and more research efforts are required to achieve this.

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