Original Article

pISSN 2383-5389 / eISSN 2383-8116

Journal of International Society for Simulation Surgery 2016;3(2):64-68 https://doi.org/10.18204/JISSiS.2016.3.2.064

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Development of Dual-Arm Anticancer Drug Compounding Robot and Preparation System with Adaptability and High-Speed

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Aim Robots are able to increase safety for pharmacy staff as separating from toxicity of anti-cancer drugs. For patient safety, it would provide right dose of the drugs. Additionally, it can reduce price of the drugs. Therefore, in this study, a novel compounding anticancer drugs robot system (Dupalro) was developed.
Methods We used the robot system, Motoman dual-arm robot from YASKAWA, Japan and medications which are adapted for the robot were constructed. In order to develop a process of compounding anticancer drugs, information about five medications that are required to make anticancer drugs in hospitals was used.
Results System for the five types of medications was constructed, and relating procedures for anticancer drugs compounding robot were developed.
Conclusion Dupalro successfully was able to not only provide incremental safety and efficiency for both patients and pharmacy staff, but also decrease price of anticancer drugs.

Key Words Dupalro · Medication · Anticancer drugs · Safety · Automatic robot · Compounding · Pharmacists.

Received: November 28, 2016, 2016 / **Revised:** November 30, 2016 / **Accepted:** December 2, 2016
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Introduction

Recently, many pharmacists who make anticancer drugs quit their job so that they avoid fatal danger. During compounding the drugs, they are exposed to a lot of toxicity which are from drugs that are required. One of risk elements is infertility (1). For the reason, female pharmacists who are exposed to the risk, especially, do not want to have responsibility to make anticancer drugs. Even though busy and large hospitals have advanced clean benches, the pharmacy staff is still exposed to danger (2, 3).

In addition, anticancer mechanisms require difficult skills, extreme carefulness, accuracy of dose, and etc. Those factors give a lot of fatigue and tiredness to the pharmacists, which results concentration difficulty (4). It makes many pharmacists require increasing their incomes with the reasons.

Many hospitals do not provide good working condition for anticancer drug compounding. Price of advanced facilities that are required to provide safety during compounding anticancer drugs is so expensive that hospitals that do not have enough funds cannot make good working conditions for pharmacists who make anticancer drugs. Also, fee of education for anticancer mechanisms is costly (5). As a result, pharmacists avoid making anticancer drugs because of its poor working condition that cannot protect their health from toxicity, caused from the compounding. Due to its expensive price of anticancer drugs, additionally, patients who cannot afford to pay the pharmacy face difficulty to get chemotherapy. Even if patients have enough money to pay antineoplastic drugs, they may not get them because the supply of them is not still enough, while demand for the drugs is high (6, 7). Therefore, insufficient supply of anticancer drugs has been issued as problem.

According to National Cancer Center in Korea, average number of cancer patients gradually increasing every year, however, average number of pharmacists who make anticancer drugs is decreasing. This factor causes the result that supply of the pharmacy is dropping, while demand of it is increasing (8).

In order to solve those problems, we developed dual arm robotic device, named as Dupalro. The robotic device is expected to provide safety for both the patients and pharmacists (9). It will increase accuracy of the pharmaceutical calculation and

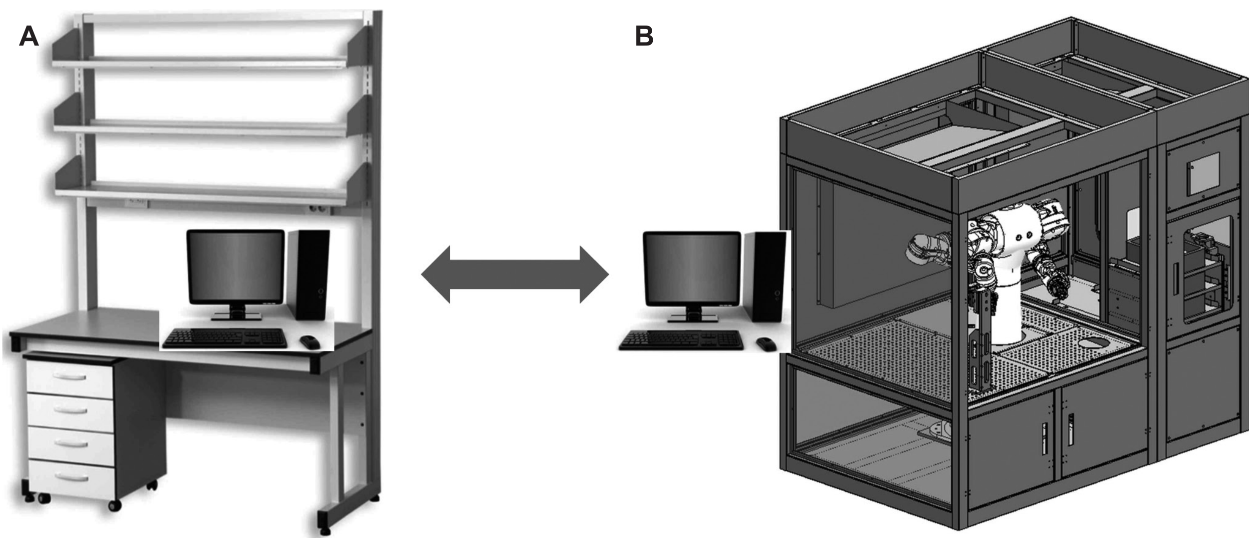

Fig. 1. In order for robotic compounding of medicine, each software and hardware part is described. A: Compounding Preparation System. B: Compounding Robot System.

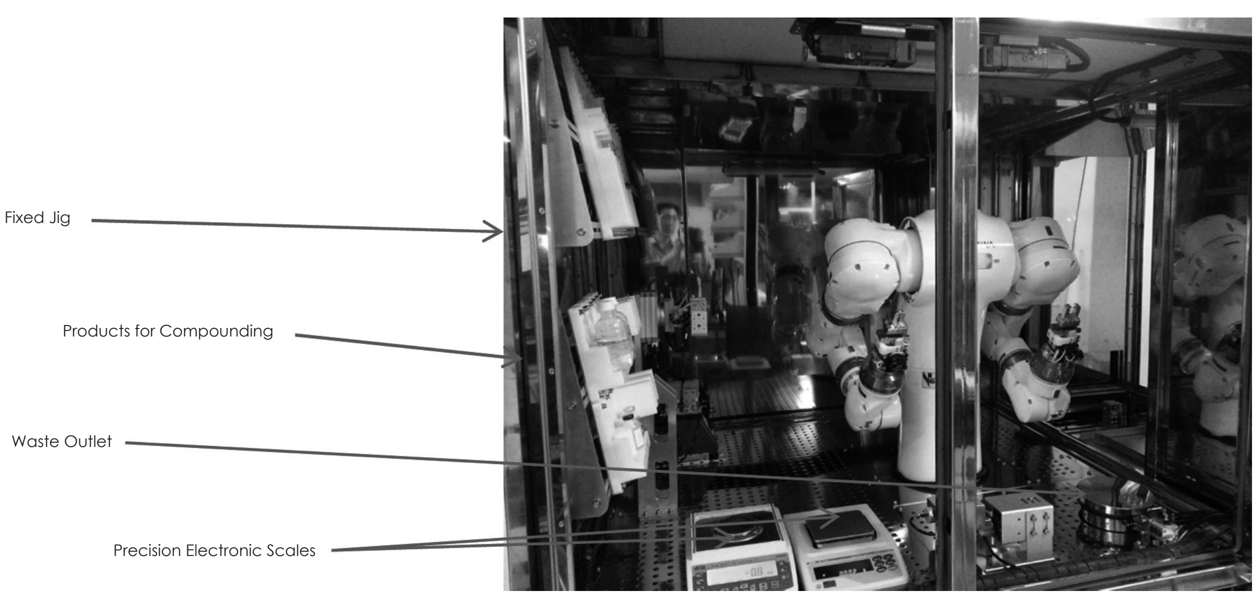

Fig. 2. Overview of DUPALRO drug robot system.

reduce error, and improve quality of anticancer drugs. Better environment can be provided to the staff as increasing time efficiency and avoiding from toxicity and danger during compounding (10). Patients who cannot afford to buy the pharmacy will be expected to get it with cheaper price. With dual arms, our compounding robot, especially, can perform faster than other compounding robots. Thus, Dupalro, dual-arm anticancer drugs compounding robot, will be helpful in diverse ways (3, 11, 12).

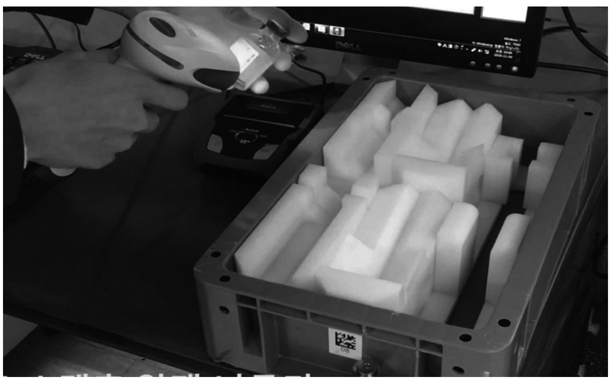

Fig. 3. Preparation for the pharmaceutical compounding in order to get information about adapted compounding drugs for patients through barcode.

Materials and Methods

A system in order to make anticancer drugs was created independently, while the robot was supplied by KAWASAKI, Japan, as OEM (Original Equipment Manufacturer). Dupalro is not same as other single-arm robot; our robotic device is dual-arm. It is strength that Dupalro is capable of working flexibly with high-speed. In addition, arms of the device were created to grip various sized vials, plastic bags and syringes, and also to press a plunger of syringe.

The basic structures of Dupalro are using stainless steel and ventilation system for air contamination and separating control system and space for compounding. The size was 2200 x 1350×2045 mm. The structure is composed of the robot and anticancer drug products supply zone and main working, testing, discharging waste, and ventilation part. At Fig. 1A, it is software system for input information about patients, relating to adapted prescription for the compounding robot. Fig. 1B is

Fig. 4. Processes of compounding drugs.

the robot system for compounding anticancer drugs. It has different system for compounding drugs with dual-arm and in addition, is relatively smaller than other compounding robots.

Fig. 2 is showing the overview of the robot system. There are parts for products for compounding, a fixed jig, a waste outlet, and a precision electronic scale.

The picture from Fig. 3 is showing that a pharmacist stores drug products for patients in a trey. When information about drugs for patients is received as EMR, pharmacists sort the products out in the trey by using the information.

For first stage, pharmacists prepare for the compound as getting information about patients. Next, the robotic device fixes syringe to the jig. It begins to weight and check products that are required to make anticancer drugs at stage 3. After, it weights water for injection to move to the next stage. The weighted water for injection is put into the syringe. The dual-arm robot weight water for injection again. Then, the syringe (water for injection) is being injected into the vial. If needed, stage 5–7 can be repeated depending on information. At last stage, the compounding robotic device mixes vials with dual-arm.

Air circulation is important because fatal toxic (cytotoxic) air is produced during compounding anticancer drugs. Ventilation system for the air contamination was composed of four pipes where are placed at each corner.

The robotic device prepares the required medicine from Electronic Medical Record (EMR) prescription to compound anticancer drug by the preparation software. Each tray has been labeled as its ID by a label printer that is connected to the software system. Next, the software system confirms whether information of a patient corresponds with the prescription. If so, it will be check that every required drug products for anticancer drug are placed on the trey. Finally, our dual arm robotic device starts compounding anticancer drug when a pharmacy press two buttons “trey preparation completed” and “allow medicine preparation.” During the process, a door of trey will not open (Safety Lock). The compounding robots, Apoteca, Cytocare, RIVA Rogbotics, KIRO Oncology, were used to analyze their performance.

Actually, hospitals use various types of products that are needed to make anticancer drugs, which mean there are diverse ways of compounding the drugs. In order to solve that problem, adapted mechanisms for the device were developed. The mechanisms were named as case 1~ case 5. Fig. 5 shows five kinds of medicine products that are needed to make anticancer drugs, which are cisplatin, doxorubicin, fluorouracil, cyclophosphamide, and ifosfamide.

This is case 1 for compounding with cisplatin (CDDP1). There are two volumes of cisplatin, 20 mL and 100 mL. In order to take 95.4 mg (190.8 mL), the robot uses two 100 mL cisplatin vials. Then, it puts 50 mL, 50 mL, 50 mL, and 41 mL into a normal saline bag through a 50 mL syringe. After carrying, it sterilizes the cap with hydrogen peroxide and then seals it.

For case 2, there are 5 mL and 25 mL of doxorubicin vials. 50 mL syringe is used to take 80 mg (40 mL) through carrying twice, 25 mL and 15 mL. After sterilization of a cap with hydrogen peroxide, it seals up the cap. Lastly, the product is diluted with 5% dextrose bag to be injected.

Three volumes of fluorouracil are checked, 5, 10, 20 mL. Only one vial of fluorouracil, 20 mL, is required to take 800 mg (16 mL) using 30 mL syringe for case 3. The label that is written the volume of the product will be attached on the syringe after putting a syringe cap.

For cyclophosphamide as case 4, 500 mg is reconstituted with 25 mL normal saline. In case of a prescription that offers 800 mg (40 mL), 25 mL vial and 15 mL vial are used to take 40 mL of cyclophosphamide and put it into s 200 mL 5% dextrose bag. Because it is non-water-soluble, it has to spend 10 minutes shaking and 30 minutes leaving at room temperature.

In case of ifosfamide, 1000 mg of it is used with 20 mL water for injection. With 50 mL syringe, two vials of 1000 mg ifosfamide (powder) are used to take 1580 mg (31.6 mL). 20 mL of water for injection (plastic) is carried into each vial, and then shake for a half minute. The mixture will be put into a 200 mL 5% dextrose bag through two vials using a syringe.

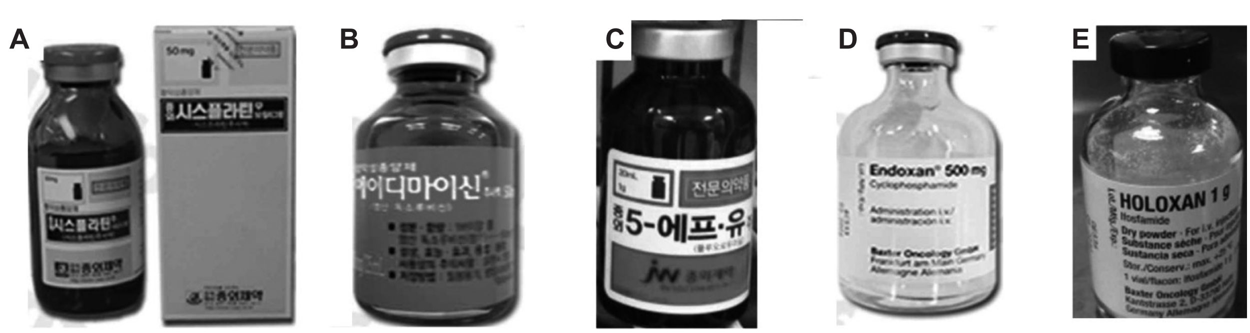

Fig. 5. A: Cisplatin. B: Doxorubicin. C: Fluororacil. D: Cyclophsphamide. E: Ifosfamide

Results

The development of software for medicine preparation and data base was successfully done with Dupalro. Additionally, compounding working processor was able to be analyzed using hospital information system. In order to test whether it worked or not, a sample prescription was analyzed and it worked very well. As dual arms, it has made anticancer drug faster than other compounding robots with single arm. Error percentage, caused from preparation of drugs was lower than other robotic devices due to its data base and software which are being developed independently. In order for compounding anticancer drugs, materials such as vial, syringe, and ringer are enough to complete the performance. A prescription of which format is used in a hospital was applied to examine the automatic compounding system, and it was expected that the system would improve the hospital working environment.

Discussion

Time taken to compound an anticancer drug with the dual-arm compounding robot, Dupalro, is relatively faster than other single-arm robotic compounding devices. However, it is still slower than a pharmacist does. It will be expected to increase efficiency for making drugs by the developed robotic device due to its continual working, though (13).

It is extremely important that the robot has to be trusted from patients and pharmacists as successfully compounding anticancer drugs. Safety also is not ignorable. There should not be any accident, caused from the device, so concentration on safety is considered as important.

Today, Samsung Hospital has applied medicine compounding robotic devices, and many other hospitals will be expected to use the compounding devices in the future, which consequently improve the quality of chemotherapy for patients.

Moreover, it needs to get clinical approval from Korea Food & Drug Administration (KFDA) in order to be applied to patients. Thus, I am expecting that Dupalro will not only be significant for chemotherapy, but also improve their quality of life as pharmacists or patients if the mentioned problems are solved.

Acknowledgements

This research was supported by a grant from the Industrial Cluster Program, Korea Industrial Complex Corporation, Republic of Korea (RDNWSU15024).

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