CHAPTER 1

INTRODUCTION

1.1 Statement of problem

Prostate cancer is the most common cancer in American men. In 2015, The American Cancer Society (ACS) has estimated that prostate cancer in the United States about 220,800 new cases will be diagnosed and about 27,540 men will die from this disease (1). The incidence rate of prostate cancer from the National Cancer Institute is the fourth after cancers of liver, lung and colorectal (2). The prostate cancer in Thailand about 4.38% new cases will be diagnosed. Moreover, this rate tends to gradually increase (3). Although the genetic and age caused prostate cancer development are still not clearly explained, dietary and behavioral risk factors are manageable (4). Therefore, changing foods and lifestyle might be the good strategy for prevention of prostate cancer in the next decade. Normally, androgen and androgen receptor (AR) are required for the development and maturation of male reproductive organs. On the other hand, in tumor initiation and progression of prostate cancer development, AR is highly active and expression. Therefore, in aging male, the controlling of AR expression or activity by dietary supplements might control the development of prostatic hyperplasia or cancer.

Purple rice (*Oryza sativa* L. *indica*) is sticky rice with purple pigment in the pericarp. It is cultivated in northern area of Thailand. The pigmented rice contains high content of phenolic compounds and anthocyanin with notable antioxidant (5). Previously, Ellagic acid, a polyphenol found in pomegranate fruit juice, suppressed AR expression resulting in the reduction of progression of prostate carcinogenesis in the transgenic rat for adenocarcinoma of prostate (TRAP) model (6). In addition, the anthocyanins extracted from black soybean could reduce prostate weight in the prostatic

hyperplasia-induced rat model (7). Anthocyanin treatment can also inhibit the growth of prostate cell xenografts in nude mice and also decrease the expression of AR and PSA in prostate cell (8). In our previous study, purple rice extract (PRE) showed anticancer in both pre and post initiation stages of colon cancer (9, 10). It also showed cytotoxic effect on the androgen-responsive LNCaP human prostate (11). However, the effects of PRE on androgen-induced prostatic hyperplasia in rat model have not been established.

Therefore, this study aimed to investigate the effect of purple rice extract on testosterone propionate-induced prostatic hyperplasia in castrated rat. To expose the mechanisms of the action, the effects of PRE on the androgen-responsive LNCaP human prostate cancer cell were examined. The supplement of purple rice extract might prevent the prostate cancer and develop for natural product which increases the value in the future.

1.2 Literature reviews

1.2.1 Prostate cancer

Prostate cancer is a malignant tumor that occurs in the prostate gland. The prostate rests below the bladder and surrounds part of the urethra. It makes fluid for semen. In young men, the size of prostate is about a walnut. As men age, the prostate grows larger. The disease is the abnormal growth of cells in prostate. It normally grows slowly and use for long time to cause any problems. The causes of prostate cancer are not known. However, the risk factors of prostate cancer are age, family history, race, and diet. Currently, the tests for prostate cancer include prostate-specific antigen (PSA) test, digital rectal exam (DRE) and biopsy.

The risk of prostate cancer increases with age. About 64% of new prostate cancer cases were diagnosed in men older than age 65 years and 23% in men older than age 75 years in the United States (12). The introduction of PSA screening caused the incidence of prostate cancer in men aged less than 50 years about 5.2% and in aged more than 75 years about 30.5% (13).

Men with a family history of prostate cancer may have a higher risk of having this disease. African-American men have a higher risk of prostate cancer than white American men. Asian men have a lower risk of prostate cancer than American men, but their risk increases if they changes socio-cultural and lifestyle (14). The incidence rates of prostate cancer in Thailand increase 3% per year between 1983-2009 (15).

Dietary factors might be related with the risk of developing prostate cancer such as high-fat diet. High-fat diet increased incidence of prostate adenocarcinomas in Lobund-Wistar rat treated with exogenous testosterone has been reported (16), while Han Jin Cho *et al.* reported high-fat diet containing lard increases prostate cancer development and progression in mice (17).

1.2.2 Hormone and prostate cancer

Androgens are hormone that controls the development and maintenance of male characteristics. The main male hormone is testosterone. It is secreted by testes of males and a small amount is secreted by the adrenal glands. In addition, testosterone is important in the development of male reproductive tissues such as the testical and prostate. Normally, testosterone is synthesized and secreted by Leydig cells of the testical. In these cells, testosterone production is regulated by luteinizing hormone (LH) and luteinizing hormone-releasing hormone (LHRH). When testosterone levels are low, the hypothalamus releases gonadotropin-releasing hormone (GnRH), which stimulates the release of FSH and LH from the pituitary gland. LH stimulates testes to produce the testosterone into blood. Testosterone transports to target tissues binding with serum sex hormone-binding globulin (SHBG) and free form enters prostate cells. Inside the cell, testosterone is converted to 5α-dihydrotestosterone (DHT) by enzyme 5α-reductase in basal epithelial cells. DHT binds to the androgen receptor (AR) with high affinity, disposes heat-shock proteins (HSPs) from the AR, and moves into the nucleus. In the nucleus, AR dimers bind to androgen response elements (AREs) in the promoter regions of target genes and to activate transcription of these genes such as prostate-specific antigen (PSA) and transmembrane protease serine 2 (TMPRSS2) leading to responses such as growth and survival as shown in Figure 1.1 (18). The increasing levels of testosterone through a negative feedback loop act on the hypothalamus and pituitary to inhibit the release of GnRH and FSH/LH, respectively.

Prostate cancer and benign prostatic hyperplasia (BPH) are linked to aging and the presence of androgens. Androgens induce the differentiation and maturation of the male reproductive organs by binding to androgen receptors. The two most important androgen hormones are testosterone and DHT. DHT is actually a more potent androgen with affinity to the androgen receptor higher than testosterone (19). It plays a significant role in the developing prostate and maintenance of homeostasis between the processes of cell proliferation and cell death. It also plays an important role in certain men's health problems, like male pattern baldness and BPH. BPH is an enlarged prostate gland, caused by an increased cellular proliferation and reduced apoptosis (20). However, several reports about androgen receptor have been linked to prostate cancer. The

androgen receptor is a type of nuclear receptor which is activated by binding of androgens. It is as a DNA binding transcription factor which regulates gene expression. In addition, AR is expressed in prostate cancers that might play a significant role in the progression of prostate cancer (21). Therefore, it has been of interest to find effective means of reducing or removing the function of the AR to prevent and treatments for prostate cancer.

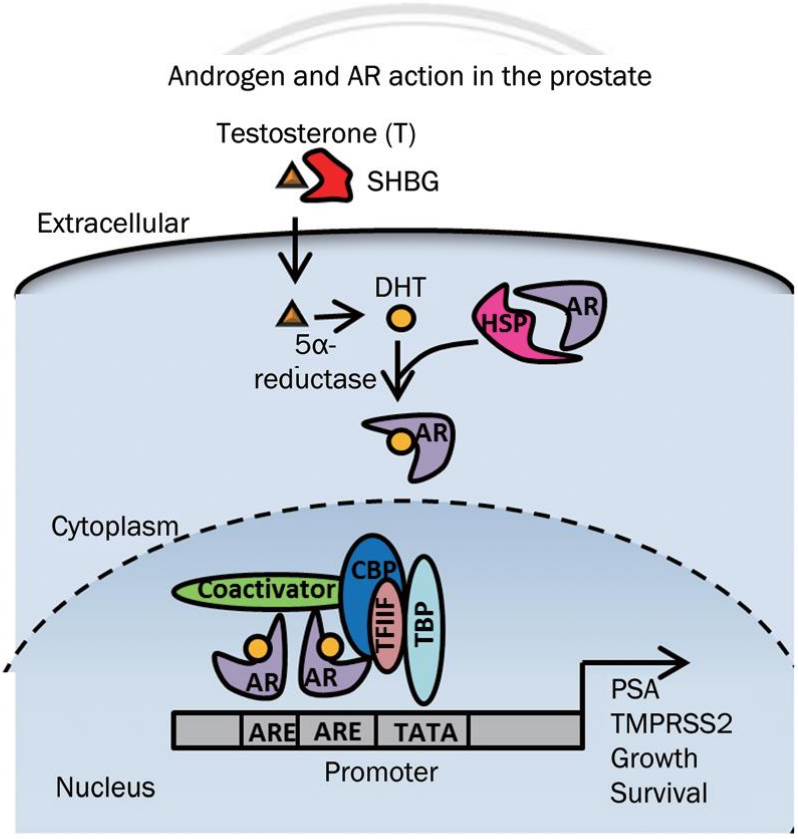

Figure 1.1 Androgen and AR signaling in prostate cells (18)

1.2.3 Treatment for prostate cancer

The effective treatments for prostate cancer are surgery, radiotherapy, chemotherapy and hormone therapy. The decision will depend on a number of factors including: Gleason score, stage of the cancer, age, side-effects of treatment and personal preference. Hormone therapy has been a mainstay for advanced prostate cancer. The aims of treatment are to reduce levels of androgens in the body or to stop them from affecting prostate cancer cells. Thus, the reduction of testosterone might help to stop growth and spread of prostate cancer. The side effects of hormone therapy are nausea, vomiting, hot flashes, anemia, lethargy and erectile dysfunction. In addition, medication to reduce the production of testosterone is luteinizing hormone-releasing hormone (LHRH) agonists, anti-androgens and drugs that prevent the production of androgens by the adrenal glands (Table 1.1) (22).

Luteinizing hormone-releasing hormone (LHRH) agonists (also known as gonadotropin-releasing hormone (GnRH) agonists) are drugs that lower the amount of testosterone made by the testicle such as leuprolide, goserelin and buserelin. Normally, GnRH is a hormone produced in the hypothalamus and transported to the pituitary gland through the blood stream. It stimulates the production of LH from the pituitary gland. Then, LH stimulates the production of testosterone in men. Therefore, LHRH agonists inhibit the release of LH and consequently less testosterone is produced (22).

Antiandrogens are drugs that block the action of androgens such as bicalutamide and flutamide. They prevent the action of androgens by blocking the receptor for androgen on the cells of the prostate gland. Bicalutamide is thought to prevent the growth of prostate cancer by blocking the effects of androgens on the cancer cells, while flutamide is a nonsteroidal antiandrogen medication that works in the same way as bicalutamide (22).

In addition to testes, testosterone is also produced by adrenal glands. Drugs prevent the adrenal glands from making androgens such as ketoconazole are applicable. These drugs block testosterone production by inhibiting an enzyme called CYP17, which is found in testicular, adrenal, and prostate tumor tissues. This enzyme plays a central role in allowing the body to produce testosterone from cholesterol (22).

In addition, 5α-reductase inhibitor is drugs that inhibit the enzyme 5α-reductase such as finasteride. 5α-reductase is the enzyme that converts testosterone into dihydrotestosterone. Because BPH and prostate cancer appear related to excess DHT production, inhibition of DHT formation within the prostate gland by 5alpha-reductase inhibitors have the effect of reducing prostate volume (22).

These hormone therapies cause many side effects which caused by the reduction of the male hormones in the body. These side effects are erection problems, hot flushes, sweating, feeling tired, breast tenderness and pain. There are other side effects that take hormone treatment for a long time such as weight gain, memory problems, mood swings and bone thinning.

Because medication or surgery affected the quality of life in older people, the prevention is the best way to reduce the BPH and prostate cancer.

Table 1.1 Hormonal interventions and endocrine axis in prostate cancer (22)

Drug class	Drugs	Mechanism of action	Risks
GnRH agonists	Leuprolide Goserelin	Decreases release of LH through down-regulation of GnRH receptors	Testosterone surge
GnRH antagonists	Abarelix	Directly inhibits GnRH receptors	Anaphylaxis
Androgen receptor antagonists	Flutamide Bicalutamide Nilutamide	Inhibits androgen receptor ligand-binding domain through competitive binding	Gynecomastia, increased liver transaminases, and mastodynia
Adrenal ablating drugs	Ketoconazole	Decreases androgen synthesis from steroid precursors through inhibition of cytochrome P450 enzymes	Administration requires steroid supplementation to prevent adrenal insufficiency
5α-reductase inhibitors	Finasteride	Decreases conversion of testosterone to DHT through inhibition of 5α-reductase	No defined role in standard care of prostate cancer

1.2.4 Prevention for prostate cancer

1) Behavior change

Prostate cancer prevention may be involved with healthy behaviors such as diet and physical activity. There are several reports about diet and lifestyle may have a role in the development of prostate cancer. In recent years, Cho *et al.* reported that high-fat diet (HFD) containing lard stimulated the proliferation and migration of prostate cancer cells and also induced body weight gain, enhanced tumor growth and progression leading to decrease in survival rate in transgenic adenocarcinoma mouse prostate (TRAMP) model (17). In addition, Leitzmann *et al.* studied the association between intakes of α-linolenic, linoleic, eicosapentaenoic, docosahexaenoic and arachidonic acids and prostate cancer risk in America men (aged 40-45 years) for 14 years. They found that a high α-linolenic intake may increase the risk of advanced prostate cancer but eicosapentaenoic and docosahexaenoic intakes may decrease the risk of advanced prostate cancer (23). In the Harvard Alumni Study (mean age 66.6 years), Sesso *et al.* studied alcohol consumption (121.1g/week) including wine (28.6%), beer (15.8%) and liquor (55.6%) for 1 drink/month to <3 drinks/week, 3 drinks/week to <1 drink/day, 1 to <3 drinks/day, and > or = 3 drinks/day compared to men never drinking alcohol (24). The result suggest that liquor consumption (ranging 3 drinks/week to <3 drinks/day) was associated with a 60% increased risk of prostate cancer. For beer, they found the reduction in prostate cancer risk at ranging from 3 drinks/week to <1 drink/day. In wine consumption was no significant associated with the risk of prostate cancers. Additionally, the study reported that physical activity reduces the risk of prostate cancer. Kenfield *et al.* results suggest that vigorous activity such as biking, tennis, jogging, or swimming for ≥3 hours a week had a 61% lower risk of prostate cancer death in men with prostate cancer (25). Consequently, diet and lifestyle modifications are a one of strategy for prostate cancer prevention. Vegetables and fruits are the most sources of antioxidants such as beta-carotene, vitamin C, vitamin E, and selenium that may help reduce the risk of developing prostate cancer, slow progression of the disease and prevent aggressive disease.

2) Role of functional food and supplementation

Phytochemicals are organic compounds found in fruits, vegetables, beans, grains and other plants such as carotenoids, phenolic acid and alkaloids. There are several reports showed that phytochemicals have effect on health benefit. The table 1.2 summarized various source phytochemicals and their preventive effects against prostate cancer in several model. In recent years, Naiki-Ito *et al.* reported that the group of polyphenols called ellagic acid found in pomegranate fruit juice prevents early stage of prostate cancer. It can decrease dorsolateral prostate weight in the transgenic rat for adenocarcinoma of prostate (TRAP) model and inhibits cell proliferation of the human prostate cancer cell (LNCaP) via induction of apoptosis by activation of caspase 3 (6). Another important polyphenols are anthocyanins found abundantly in bright red, blue and purple colors of fruits and vegetables (such as berries, grapes, apples, purple cabbage and corn), which have been shown to inhibit the development of various cancer in animal model studies such as esophageal cancer, colon cancer, skin cancer and lung cancer (26). In addition, Jang *et al.* reported that anthocyanins extracted from black soybean could reduce prostate weight in the prostatic hyperplasia-induced rat model (7). Therefore, the study of plants which contained high polyphenol especially anthocyanin might be the inhibition of target natural product that could be applied for inhibition of prostate hyperplasia.

Table 1.2 Types of phytochemicals and prevention effects

Plant	Phytochemical	Biological activity
Black soybean extract	Anthocyanin	Reduce prostate weight and promote apoptosis in the prostatic hyperplasia-induced rat model (7)
Ginger extract	Gingerols, paradols, shogaols and gingerones	Inhibit prostate cancer cells and inhibit growth and progression of PC-3 xenografts (27)
Grape seed extract	Procyanidins	Induce apoptotic death of human prostate cells (28)
Green tea extract	Epigallocatechin-3-gallate	Promote apoptosis in prostate cancer cells and reduce gene expression and protein expression of AR in LNCaP cell (29)
Pao pereira extract	β- carboline alkaloid	Reduce tumor cell proliferation and xenograft growth in mice xenografted with LNCaP cells (30)
Pomegranate extract	Ellagic acid	Decrease dorsolateral prostate weight in the TRAP model and inhibits cell proliferation of LNCaP cell via induction of apoptosis by activation of caspase 3 (6)
Soy extract	Isoflavones	Delay progression of prostate cancer from benign to malignant tumors in TRAMP model (31)

1.2.5 Purple rice and health benefit

Rice (*Oryza sativa*) is an important staple food crop for Asian diet. It is composed of carbohydrates, with small amounts of protein and nearly no fat. In addition, it also has high vitamins and other minerals. The pigmentation in the bran of rice has many different colors including brown, red, purple and black. These colorful rice varieties are often prized for their health properties. Purple rice (*Oryza sativa* L. indica) is cultivated widely in different regions of Thailand. It also has been used as a traditional Thai herb for medical treatment. The chemical components of purple rice are anthocyanin, gamma-oryzanol and vitamin E derivatives (32). Purple rice contains anthocyanin glycosides such as cyanidin-3-glucoside, cyanidin-3-rhamnoglucoside, malvidin-3-galactoside and peonidin-3-glucoside that are not contained in other types of rice as shown in Figure 1.2 (33). Anthocyanins are a subunit substance of flavonoids. These compounds are reported to have potentially beneficial effects including vasoprotective and anti-inflammatory (34) as well as antioxidant and chemoprotective properties (35). Recent study, isoflavones and anthocyanin in seoritae extract can reduce prostate weight and suppresses prostate cell proliferation in a rat model of benign prostate hyperplasia (36). Furthermore, previous studies have reported that cyanidin-3-glucoside exerts anti-tumor activity in ovarian cancer (37). An *in vivo* study showed that an anthocyanin mixture from bilberry and isolated cyanidin-3-glucoside can prevent carcinogen-induced colorectal cancer in rats (38). Another study found that isolated the cyanidin-3-glucoside and peonidin-3-glucoside from Oryza sativa *L. indica* and tested their effects on various cancer cells. They found that two phytochemicals have strong inhibitory effects on cell growth of highly metastatic breast cancer cells (HS578T) and this effect involving alterations in cell cycle regulators to result in G2/M arrests (35). In addition, gamma-oryzanol is an antioxidant able to inhibit prostate cancer cells (DU145 and PC3) through the down regulation of some antioxidant genes, CAT and GPX (39).

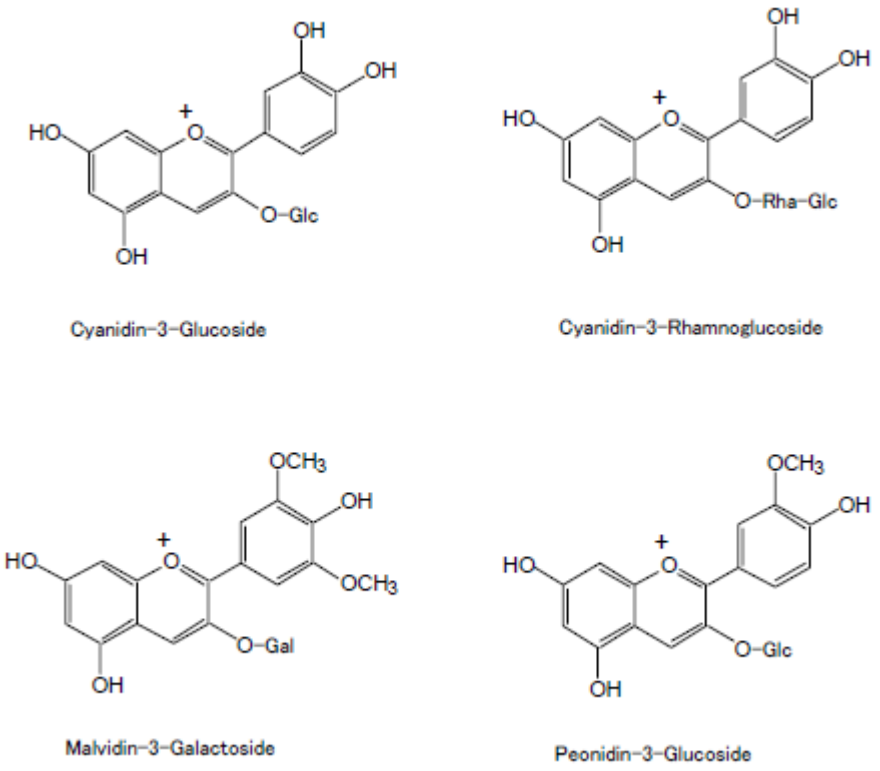

Figure 1.2 Major components of purple rice extract (33)

Northern Thai purple rice has collected and developed by Purple Rice Research Unit (PRRU), Faculty of Agriculture, Chaing Mai University. Of 31 varieties of landrace purple rice contained high total phenolic compound compared to White rice varieties KDML 105 and RD6 as shown in Table 1.3 (40). In addition, purple rice or Khao Kum contained high amount of total anthocyanins, antioxidant activit, GABA (gamma-aminobutyric acid), gamma-oryzanol and vitamin E derivatives especially Kum Doi Saket strains as shown in Table 1.4-1.6 (41-43). Previous studies reported that the crude proanthocyanidin extract of purple rice Kum Doisaket have an anticancer effect on plasma cancer cells of mice (X63) (44). Furthermore, purple rice Kum Doisaket extract had the highest level of antimutagenicity in a *Salmonella* mutation assay. Punvittayagul *et al*. found that purple rice extract had no acute toxicity on rats and significantly reduced the amount of micronucleus formation in the liver of diethylnitrosamine (DEN)-treated rats (45). In addition, purple rice extracted (Kum Doisaket) presented cytotoxic effects on LNCaP cells (11). Purple rice Kum Doisaket

extracts can inhibit colon carcinogenesis in both post-initiation and progression state in rats model. According to the properties and biological activity of purple rice extract (Kum Doisaket) led to an interesting study the effect on prostate cancer prevention. Therefore, the testosterone-induced prostatic hyperplasia in rat model will be performed. Then, molecular mechanisms of purple rice extract will be investigated in human prostate cancer cell line. The supplement of purple rice extract might prevent the prostate cancer and develop for neutral product for prostate cancer prevention

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Table 1.3 Total phenolic compound contents in rice (40)

Varieties	Total Phenol (mg/g GE)	Pericarp	Varietiy	Total Phenol (mg/g GE)	Pericarp
S0902	10.86[a]	dark purple	Kum 87061	4.20[i]	purple
S0903	10.36[b]	dark purple	Kum 99151	4.08[j]	purple
S0907	7.72[c]	dark purple	Kum 88069	4.08[j]	purple
S0904	7.03[d]	dark purple	Kum 89057	3.94[j]	purple
S0905	6.09[e]	dark purple	Kum Vietnam	3.54[k]	purple
Kum Doi Saket	5.26[f]	dark purple	Kum 7677	2.91[n]	purple
Kum Nan	5.25[f]	dark purple	Kum 5153	2.55[q]	purple
S0901	5.25[f]	dark purple	Kum 87090	2.51[r]	purple
Kum Phayao	5.24[f]	dark purple	Kum 19959	3.73[k]	light purple
S0908	4.84[g]	dark purple	Kum Fang	3.28[l]	light purple
Kum Doi Moosour	4.25[i]	dark purple	Kum19104	3.12[m]	light purple
S0906	3.09[m]	dark purple	Kum Na	2.80[o]	light purple
Kum Supan	6.14[e]	purple	Kum Wiengsa	2.72[p]	light purple
Kum 89038	6.00[e]	purple	Purple rice mean	4.48	
Kum 88061	5.02[g]	purple	KDML 105	0.75[s]	brown
Kum Hoksalee	4.96[g]	purple	RD 6	0.65[s]	brown
Kum 88083	4.62[h]	purple	$LSD_{0.05}$	0.20[**]	
Kum 87046	4.20[i]	purple	CV.	2.57	

Table 1.4 Comparison of quantitative components from two purple glutinous rice varieties (Kum Doi Saket and Kum Phayao). (41)

Qualities	Unpolished purple glutinous rice[1/]	
	Kum Doi Saket	Kum Phayao
Physical composition		
Germination rate (% of grains)	90.33 [a] ± 1.52	81 [b] ± 1.00
Chemical compositions		
Moisture (%)	10.78 [b] ± 0.02	11.42 [a] ± 0.07
Protein (%)	8.56 [a] ± 0.09	6.89 [b] ± 0.06
Fat (%)	2.57 [a] ± 0.12	2.12 [b] ± 0.16
Ashns (%)	1.40 ± 0.07	1.47 ± 0.10
Crude fiber (%)	1.86 [a] ± 0.18	1.60 [b] ± 0.12
Carbohydrate (%)	74.83 [a] ± 0.07	76.50 [b] ± 0.19
Reducing sugarns (%)	0.22 ± 0.01	0.26 ± 0.02
Amylose (%)	1.86 [a] ± 0.18	1.60 [b] ± 0.12
Bioactive compounds		
GABA (mg/100g DW)	0.85 [a] ± 0.01	0.60 [b] ± 0.02
Gamma-oryzanol (mg/100g DW)	22.55 [a] ± 1.81	18.51 [b] ± 1.73
Total anthocyanin (mg/100g DW)	117.19 [a] ± 2.30	78.48 [b] ± 1.02
Antioxidant activity		
DPPH scavenging activity (%)	90.97 [a] ± 0.52	75.83 [b] ± 0.96

Note: [1/]For the comparison in each row, the different letters indicated the statistically significant difference ($p<0.05$). ns not a significant difference.

Table 1.5 Crude oil, semi gamma oryzanol and gamma oryzanol content (42)

Collection	**Crude oil** (g/100g grain)	**Semi purified γ-oryzanol** (g/100g grain)	**γ-oryzanol** (mg/100g grain)
Purple rice			
Kum Doi Musur	2.85ab	2.24ab	75.30a
Kum Doi Sa Ket	2.43bc	2.15abc	74.84a
Kum Nan	2.68abc	2.27ab	73.62a
Kum 7677	2.64abc	2.18ab	62.30b
Kum 87061	2.23c	1.85d	60.48b
Kum Vengsa	2.47bc	2.08bcd	59.89b
Kum 19959	2.91ab	2.40a	57.50b
Kum 99151	2.73abc	2.36a	49.14c
Kum19104	2.20c	1.88cd	48.10cd
Kum 88061	2.21c	2.07bcd	43.74de
Kum 89038	2.37bc	2.04bcd	42.21e
Kum Na	2.91ab	2.27ab	40.47e
Kum Omkoi	2.19c	2.07ab	39.84e
White rice			
KDML 105	3.09a	2.16ab	30.89f
RD6	2.93ab	1.81d	30.44f
mean	2.59	2.12	52.58
$LSD_{0.05}$	0.62*	0.27*	5.30*
SE	2.59	0.30	0.13

Table 1.6 Crude fat and vitamin E (Tocopherols) contents in rice bran (43)

Purple rice genotype	Crude fat (% of seed mass)	Antioxidant content (µg/g dw)			
		Tocopherols			
		α	β	γ	Total
Kum Phayao	6.23 hijklm	37.57	49.55	119.58	206.69 b
Kum Wiengsa	19.58 cd	22.75	24.10	55.59	102.44 lk
Kum Na	17.44 fg	59.88	50.12	144.07	254.07 a
Kum Nan	17.2 fgh	14.63	26.09	65.16	105.88 klm
Kum DoiSaKet	19.82 cd	26.68	30.84	83.82	141.38 efghi
Kum Hoksalee	17.72 ef	13.62	23.34	88.36	125.31 ghijkl
Kum DoiMoseur	20.06 c	20.59	29.43	57.18	107.21 jklm
Kum Fang	15.75 klmn	22.73	39.22	87.05	149.0 defg
Kum 5153	16.16 hijklm	24.85	29.32	117.70	171.86 cd
Kum 7677	14.10 o	16.98	36.54	83.67	137.19 efghi
Kum 87061	14.81 no	20.40	29.53	93.67	142.96 efgh
Kum 87090	18.85 de	29.84	26.82	105.23	161.89 de
Kum 87046	16.08 hijklm	19.63	25.15	84.27	129.05 fghijk
Kum 89038	15.57 lmn	20.19	25.28	92.99	138.47 efght
Kum 89057	14.36 o	17.94	28.70	69.74	116.38 ijkl
Kum 88061	16.30 hijklm	17.49	30.88	83.05	131.42 fghij
Kum 88069	16.72 hijklm	31.63	24.02	75.35	130.99 fghij
Kum 88083	16.05 ijklm	15.08	19.62	72.57	107.27 jklm
Kum 99151	16.42 ghijkl	20.63	24.28	63.61	108.53 jklm
Kum 11875	20.59 c	9.67	19.18	59.05	87.90 m
Kum 19104	16.96 fghij	37.44	48.87	106.03	192.33 bc
Kum 19959	17.09 fghi	18.62	22.86	69.62	111.10 jklm
Kum Supan	15.19 mno	18.17	32.21	76.67	127.06 ghijkl
Kum Vietnam	15.86 jklmn	27.70	29.13	97.11	153.93 def
(White rice)					
RD6	23.00 b	19.01	0.0	105.48	124.49 ghijkl
KDML105	24.68 a	18.13	1.54	98.90	118.57 hijkl

1.3 Objective

1.3.1 To investigate the effect of purple rice extract on testosterone-induced prostatic hyperplasia in rats

1.3.2 To investigate the mechanism of purple rice extract on expression of androgen receptor, target gene of androgen receptor and proteins involved in cell growth of prostate cancer cell