Volume 20, No 4 | International Journal of Radiation Research, October 2022

Impact of cherry juice on oxidative stress and fertility impairment in aged irradiated rats

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► ***Original article***

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Received: June 2021
Final revised: May 2022
Accepted: May 2022

Int. J. Radiat. Res., October 2022; 20(4): 799-806

DOI: 10.52547/ijrr.20.4.11

All authors are contributed equally to this work. Approval for experimental study 2-5-2018.

Keywords: *radioactive Aging rats, STAR, testosterone, estrogen, γ-irradiation.*

ABSTRACT

***Background*:** This study targeted to conclude the effect of cherry juice and fractionated dose γ-irradiation on the fertility of elderly rats. ***Materials and Methods*:** Male and female rats were assigned to five groups: young adult control, old adult control, old adult irradiated using ^{137}Cs, source (0.3 Gy*3), old adult cherry juice and cherry irradiated group. Cherry juice was administered orally at the dose 5ml/kg b.w. Follicle stimulating hormone (FSH), estradiol (E2), 8-hydroxy-2-deoxyguanosine (8-OHdG), and insulin-Like Growth Factor 1 (IGF-1) were estimated in the serum of female rats. Serum testosterone (T), FSH, and testicular steroidogenic acute regulatory (STAR) gene expression were evaluated in male rats. Metallothionine (MT), malondialdehyde (MDA) and glutathione (GSH) were estimated in the uterus and testes. ***Results*:** Co-treatments of old adult male and female rats with cherry juice and fractionated doses of γ-irradiation developed a significant decrease in MDA in uterus and testes, parallel with an increase in the level of uterus MT and testes GSH as compared with young rats. A significant increase in the levels of female E2, IGF-1, and male T along with a decrease in FSH in both sexes was observed. Additionally, STAR gene expression in male was up regulated. ***Conclusion*:** Fractionated dose of gamma radiation (0.3 Gy*3) has no effect on tested reproductive hormones, while Cherry juice stimulates the secretion of E2, and T, and elevates GSH. Tart cherry juice can improve reproductive ability, especially for those undergoing radiotherapy Thus, cherry juice may be a potential candidate to ameliorate the effect of aging on reproductive ability.

INTRODUCTION

Aging is a complicated biological process involving the accumulation of variations over a long life span. These changes include biological, physical, and biochemical processes that can cause dysfunction in cells and organs [1]. Age-related alterations in mitochondria lead to debility in mitochondrial function. By age, mitochondrial DNA size and functionality decline because of reactive oxygen species (ROS) increase mutations and oxidative impairment [2]. Cellular senescence may increase an innovative decline in female reproductive ability by declining the oocytes quality [3]. Loss of fertility may be due to the lack of follicles or the incapability of the remaining follicles to respond to stimulation [4]. Aging of male reproductive organ usually accompanied with a fall in serum T [5], reduced muscle strength, reduced libido, and declining fertility [6]. Oxidative stress also increases with aging [7], which can damage cellular macromolecules via oxidation of deoxyguanosine to 8 -OHdG and result in mutations of mitochondrial DNA [8].There are numerous pathways of DNA repair, which depend on the type of DNA damage. Base excision repair (BER) is the chief pathway for repair of minor DNA alterations [9]; however, the capability of BER to restore DNA declines by age [10].

Although high doses of ionizing radiation are detrimental, studies of both humans and experimental animals show that low dose radiation stimulates biological functions [11], such as a radio-protective response [12], activation of the immune system [13], stimulation of the radical detoxification system, enhancement of DNA repair rates, and an induction of the immune capability that is concomitant with the rise in the quantity of cytotoxic lymphocytes. Low dose radiation can also, decrease the incidence of metastatic cancer [14]. In contrast Cong-Shu Huang *et al.* conveyed that 0.5-Gy gamma rays exert notable DNA damage, cycle arrest, apoptosis, and altered serum testosterone level in mice [15].

Anthocyanins are compounds belonging to the bigger flavonoids class that include a subgroup of the polyphenol class of compounds. Main sources of anthocyanins are blueberries, cherries, raspberries, strawberries. Anthocyanins are absorbed from the stomach and the small intestine and reaching maximum after 2 hours [16]. Some ingested anthocyanin is absorbed, circulated in the plasma,

[DOI: 10.52547/ijrr.20.4.11]

and delivered into the urine without undertaking metabolic alterations [17]. Anthocyanins and further phenolic compounds existing in tart cherries possess antioxidant and anti-inflammatory properties [18]. Moreover, tart cherry anthocyanins and cyanidin may diminish the danger of colon cancer [19] and diminish inflammation-induced thermal hyperalgesia, and paw edema [20]. Anthocyanin treatment of the varicocele showed a significantly increase testes weight, sperm motility, and spermatogenic cell density, with a decrease in apoptosis body count [21]. Additionally, Jang *et al.* [22] reported that anthocyanin supplementation may prevent excessive speedy cell death in the prostate from apoptosis in an animal model of andropause. Utamia *et al.* [23] reported that the high dose of anthocyanin in the purple variety of sweet potatoes prevents the reduction of estrogen receptor α expression and prevents endometrium thinning in white rats exposed to cigarette smoke. A previous study showed that rats with age-related impairments that had a tart cherry-supplemented diet showed improvement in behavioral and neuronal function [24]. There is evidence that cherries can be used as a preventive health measure by countering exposure to mutagens [25]. Therefore, this work aimed to investigate the enhanced impact of cherry juice on the fertility of aged and aged irradiated rats with the goals of ameliorating deterioration from aging and improving reproductive ability and quality of life.

MATERIALS AND METHODS

Treatment

Cherry juice concentrate with anthocyanin complex was obtained from Nature's Goodness (Australia Pty, Ltd.). The ingredients were tart cherry pure (45%), sweet cherry puree (45%), cherry juice concentrate (10%), and anthocyanin complex concentrate (0.5%).

Animals

Old adult male (OAM) (350-400 g) and old adult female (OAF) albino rats (250-300 g) and young adult male (YAM) and young adult female (YAF) rats (120-150 g) were attained from the National Centre for Radiation Research and Technology (NCRRT) in Cairo, Egypt. Rats were contained in consistent cages and kept in proper aeration, at a temperature of 25˚C ± 3˚C, 60% moisture, with appropriate lighting surroundings (light/dark cycle), and they were permitted a normal tablet food and renewed water *ad libitum*. Animals were given one week to acclimate to the lab situation afore the beginning of the experiment.

Irradiation process

Each rat's whole body was γ-irradiated using ^{137}Cs, source (γ-Cell-40) located in the NCRRT. The dose rate was 0.43 Gy/min at the stage of the experiment. The animals were exposed to a fractionated dose of γ-rays, 0.3 Gy/week for 3 weeks (a total of 0.9 Gy).

Experimental design

For male and female: Fifty rats were divided into 10 groups, five rats per group (5 groups for each sex).
Group I: Young adult control (YAF and YAM): Reference group for comparison between young (4 months) and old rats (18- 20 months) for evaluating the remedial effect of cherry juice and/ or γ-irradiation.
Group II: Old adult control (OAF and OAM): Aging rats (18-20 months) that did not receive treatment.
Group III: Irradiated group (Rad): Old adult rats that were exposed to 0.9 Gy delivered as 0.3 Gy/week for 3 weeks.
Group IV: Cherry group (Ch): Old adult rats that were orally administrated cherry (5 ml/kg b.wt.) daily for 3 weeks (26).
Group V: Cherry irradiated group (Rad + Ch): Old adult rats treated with γ-irradiation (0.3 Gy/week for 3 weeks) together with cherry (5 ml/kg b.wt. daily for 3 weeks).

Reproductive process

For each group, two cages assigned to reproductive process each contained one male and four female (totally 10 male and 40 females).

Sampling process

After a 24 h post- treatment period, rats were anesthetized by urethane (1.2 mg/kg b.wt.)(27) and then sacrificed. Blood was collected by heart puncture for obtaining serum, uteri, and ovaries, and testes were collected. The ovaries, uteri, and testes samples were homogenized (1:5 w/v) in 0.9% saline for biochemical assays. Two ovaries of each group were immediately fixed in 10% formalin for histopathological investigation.

Biochemical assay

Metallothionine was evaluated in the uterus and testes with the Ag-saturation hemolysate technique agreeing to Scheuhammer and Cherian [28] and Bienengräber *et al.* [29] by a Thermo Scientific iCE 3000 SERIES for atomic absorption spectrometry. Malondialdehyde (MDA) and glutathione content (GSH) were measured in the uterus and testes homogenate according to Yoshioka *et al.* [30] and Beutler *et al.* [31], respectively. All chemicals used were an analytical evaluation and purchased from Sigma-Aldrich. Rat follicle stimulating hormone (FSH) (Cat No. MBS720215) was measured in the serum of male and female rats, as well as serum E2 (Cat No. MBS702969) and 8-OHdG (Cat No.MBS269902) were measured in the serum of female rats. The male T (Cat No. MBS282195), and the ovarian rat- insulin-

[DOI: 10.52547/ijrr.20.4.11]

like growth factor (IGF-1) (CAT NO. MBS2501249), were measured conferring to manufacturer's directions for the commercial enzyme-linked immunosorbent assay (ELISA) kit for rats (MyBioSource Co., USA).

RNA extraction and reverse transcription polymerase chain reaction (RT-PCR) analysis for testicular steroidogenic acute regulatory (STAR) in testes

Total RNA was sequestered from testes homogenate by RNase (Ribonuclease) Purification Reagent (Qiagen, Valencia, CA) agreeing to the producer's protocol. Extracted RNA was calculated via spectrophotometer at 260 nm. Reverse transcription was done on 5µg RNA sample by Moloney murine leukemia virus (M-MuLV) reverse transcriptase in a 50µL reaction volume. Mixtures of the reverse transcription were used for extension of STAR fragments by PCR by the primer pairs recorded in table 1.

Table 1. Sequences of polymerase chain reaction (PCR) primer pairs.

Genes	Primer
STAR NC_051351.1	Forward primer: 5′-GGGCATACTCAACAACCAG-3′ Reverse primer: 5′-ACCTCCAGTCGGAACACC-3′
GADPH NC_051347.1	Forward primer: 5'-CTCCCATTCTTCCACCTTTG-3' Reverse primer: 5'-CTTGCTCTCAGTATCCTTGC-3'

The expression altitudes of all transcriptions were controlled to glyceraldehyde-3-phosphate dehydrogenase (GAPDH) mRNA. The real time PCR was done by the QuantiTect SYBR green PCR Kit (Qiagen, Germany) agreeing to the producer's instructions (Applied Biosystems 7500 Instrument, USA). Relative expression of the STAR gene was deliberate by means of the relative threshold cycle routine. All values were standardized to GADPH gene. The comparative amount was measured by the expression $2^{-\Delta\Delta Ct}$ [32].

Histopathological studies

Ovary and testes were fixed in 10% formalin, splashed, and dried. The dry samples were then washed in xylene, fixed in paraffin masses, and divide up at 4-6µm thick, deparaffinized via xylol and stained by hematoxylin and eosin (H&E) [33]. Slide tissue sections were observed by light microscope: Olympus xc30, Tokyo, Japan.

Statistical analysis

Records are conveyed as means ± standard error of the mean (SEM). $P < 0.05$ was significantly different for all experiments according to one- way analysis of variance (ANOVA), and Tukey-Kramer test multiple comparisons were done via Instant software, v.5 (GraphPad Inc., San Diego, CA, USA).

Results

Reproductive process evaluation

Before starting treatment, 100% of YAF rats and 75% of OAF rats became pregnant at approximately the same time. The giving born of OAF was 50% of neonatal compared with YAF. Treatment was carried out on OAF only. Seventy-five percent of cherry- treated OAF rats became pregnant; whereas only 50% of control OAF rats became pregnant at the same time. The number of rats that gave birth was 7.2±0.37 for the YAF group, 4.2±0.36 for OAF and 4.8 ±0.38 for the old adult cherry treated group (Ch group). Conversely, γ-irradiated rats and γ-irradiated rats which received cherry did not give birth.

Female biochemical evaluation

Determination of serum E2, FSH, and ovarian IGF-1

Statistics disclosed that there was a major decline in the E2, IGF-1 levels with a significant rise in the level of FSH in the OAF as equated to the YAF group. However, OAF that received cherry extract (Ch group) had a significant elevation in E2 and IGF-1 levels when compared to the OAF group. OAF exposed to gamma radiation alone (0.3 Gy*3) showed insignificant effect on the tested parameters. Moreover, co-therapy (Rad+ Ch) treatment significantly ameliorates the levels of E2, IGF-1, and FSH when compared to the OAF and irradiated groups (table 2).

Table 2. Effect of cherry extract on estradiol (E2), follicle stimulating hormone (FSH), and ovarian insulin-like growth factor (IGF-1) in old irradiated female rats.

Groups	E2 (pg/ ml)	FSH (ng/ ml)	IGF-1 (pg/ g tissue)
YAF	10.60± 1.068	7.25± 0.621	103.0± 4.40
OAF	2.63± 0.103[a]	13.43± 1.32[a]	67.28± 4.06[a]
Rad	4.03± 0.312	16.55± 1.06	64.50± 4.52
Ch	8.35± 0.456[b]	12.93± 0.970	90.75± 2.91[b]
Rad+ Ch	7.00± 0.253[bc]	9.40± 0.320[bc]	87.98± 4.24[bc]

Data represented as mean ± standard error (SE). YAF: young adult female, OAF: old adult female, Rad: irradiated, Ch: cherry. [a]Significantly different from YAF. [b]Significantly different from OAF. [c]Significantly different from irradiated group. $P \leq 0.05$ Statistical analysis was by one-way analysis of variance (ANOVA) followed by Tukey- Kramer Multiple Comparison Test.

Determination of female oxidative stress parameters

The old female group showed a significant elevation in 8-OHdG and MDA along with a decrease in GSH with no change in the level of metallothionine (MT) paralleled to the YAF group. The irradiated group showed a significant decrease in the level of 8-OHdG with no change in the other measurements as compared to the OAF. Rats treated with cherry had a significant increase in the level of 8-OHdG and MT as compared to OAF. Furthermore, rats treated with Ch in combination with γ-irradiation had a significant amelioration in 8-OHdG and MDA levels when compared to the OAF (table 3).

[DOI: 10.52547/ijrr.20.4.11]

Table 3. Effect of cherry extract on 8-hydroxy-2 deoxyguanosine (8-OHdG), malondialdehyde (MDA), glutathione (GSH), and metallothionine (MT) levels in old irradiated female rats.

Groups	8-OHdG (pg/g ovary)	MDA (nmol/g uterus)	GSH (µg/g uterus)	MT (ug/g uterus)
YAF	2.86±0.109	19.85±1.738	243.6±18.17	5.135±0.481
OAF	18.3±0.990[a]	31.73±1.863[a]	149.7±1.281[a]	6.702±0.472
Rad	11.23±0.429[b]	30.95±2.712	170.4±12.31	5.168±0.490
Ch	14.00±0.918[b]	32.58±3.239	176.0±14.17	10.43±0.842[b]
Rad+ Ch	13.33±1.115[b]	21.14±1.169[bc]	129.5± 7.22	7.911±0.268[c]

Data represented as mean ± standard error (SE). YAF: young adult female, OAF: old adult female, Rad: irradiated, Ch: cherry. [a]Significantly different from YAF. [b]Significantly different from OAF. [c]Significantly different from irradiated group. P ≤0.05 Statistical analysis was by one-way analysis of variance (ANOVA) followed by Tukey- Kramer Multiple Comparison Test.

Male biochemical evaluations

Determination of serum T, FSH hormones, and STAR gene expression

As shown in table 4, the level of T significantly fell in the OAM group with a significant rise in the FSH level as compared to the YAM group. Additionally, the irradiated group recorded a significant increase in the FSH level without any change in T level compared to the OAM group. Treatment of OAM rats with cherry extract and/or irradiation ameliorated the T and FSH levels when compared to the OAM and irradiated groups, the more pronounced effect was observed in the group treated with both cherry extract and irradiation. The old male group had a decrease in STAR expression when compared to the YAM, while old male rats exposed to γ-irradiation exhibited no significant change of STAR gene expression when compared to the OAM. However, Ch and Rad+Ch groups recorded significant amelioration in STAR expression when compared to OAM and irradiated groups.

Table 4. Effect of cherry extract on serum testosterone (T), follicle stimulating hormone (FSH), and testicular steroidogenic acute regulatory (STAR) gene expression in irradiated male rats.

Groups	T (ng/ml)	FSH (ng/ ml)	STAR
YAM	7.42±0.446	2.85±0.174	1.02±0.010
OAM	4.52±0.161[a]	9.15±0.702[a]	0.315±0.081[a]
Rad	5.23±0.436	5.56±0.490[b]	0.5±0.030
Ch	7.73±0.225[b]	4.30±0.189[b]	0.83±0.054[b]
Rad+ Ch	7.07±0.135[bc]	3.60±0.144[bc]	0.910±0.026[bc]

Data represented as mean ± standard error (SE). YAF: young adult female, OAF: old adult female, Rad: irradiated, Ch: cherry. [a]Significantly different from YAF. [b]Significantly different from OAF. [c]Significantly different from irradiated group. P ≤0.05 Statistical analysis was by one-way analysis of variance (ANOVA) followed by Tukey- Kramer Multiple Comparison Test.

Determination of testicular oxidative stress parameters

There was a significant reduction in testicular GSH concentration and a significant elevation of MDA and MT concentration in OAM when compared to YAM. Irradiation produced a significant lessening in the GSH and MT levels and a non- significant alteration in MDA level when compared to OAM. Administration of cherry to old rats ameliorates the MDA when compared to the old control group; however, administration of cherry extract to the irradiated old rats caused an elevation in GSH when compared to OAM and the irradiated group, with a significant decrease in MDA concentration as compared to OAM. Cherry and/or γ-irradiation exposure had no significant effect on MT when compared to OAM (table 5).

Table 3. Effect of cherry extract on 8-hydroxy-2 deoxyguanosine (8-OHdG), malondialdehyde (MDA), glutathione (GSH), and metallothionine (MT) levels in old irradiated female rats.

Groups	MDA (nmol/ g tissue)	GSH (µg/ g tissue)	MT (ug/ g tissue)
YAM	25.95± 0.927	698.3± 45.10	17.55 ± 0.545
OAM	36.15± 0.94	488.6± 41.22[a]	29.28 ± 1.30[a]
Rad	32.4± 1.17	299.0± 16.38[b]	21.62 ± 1.88[b]
Ch	31.20± 0.054[b]	521.7± 39.12	27.52 ± 0.415
Rad+ Ch	22.74± 1.25[b]	617.4± 28.65[bc]	25.10 ± 1.73

Data represented as mean ± standard error (SE). YAF: young adult female, OAF: old adult female, Rad: irradiated, Ch: cherry. [a]Significantly different from YAF. [b]Significantly different from OAF. [c]Significantly different from irradiated group. P ≤0.05 Statistical analysis was by one-way analysis of variance (ANOVA) followed by Tukey- Kramer Multiple Comparison Test.

Histopathological examination

The young female control group showed a normal histological structure of the different stages of the follicles (Fs) with CL (3.5±0.29), as recorded in figure 1A. Moreover, the old female control group presented a normal histological structure of the different stages of the follicle (Fs), CL (7±0.4), and interstitial stromal cells (st) as shown in figure 1B. While the irradiated group had multiple numbers of the CL (11.75±0.47) with massive interstitial stromal cells (st), fewer follicles (Fs) were detected in both the cortex and medulla, as shown in figure 1C. However, the cherry group showed no significant change in the ovary structure, indicating normal histological structure of different stages of follicles (Fs) and CL (8 ± 0.4) (figure 1D). The Rad+Ch group showed no histological change, observing different stages of the follicles (Fs) with (20 ± 0.4), as recorded in figure 1E.

Testes of the young male control showed that there was average histological construction of mature active seminiferous tubules with whole spermatogenic series (figure 2A). Old control group recorded the same results as young as shown in figure 2B. Irradiated group observed degeneration with loss of spermatogenesis and calcification in some individual seminiferous tubules (figure 2C). Cherry group showed normal histological structure of seminiferous tubules (figure 2D). Irradiated rats treated with cherry exhibited congestion in the interstitial stromal blood vessels with homogenous eosinophillic transudation (figure E).

[DOI: 10.52547/ijrr.20.4.11]

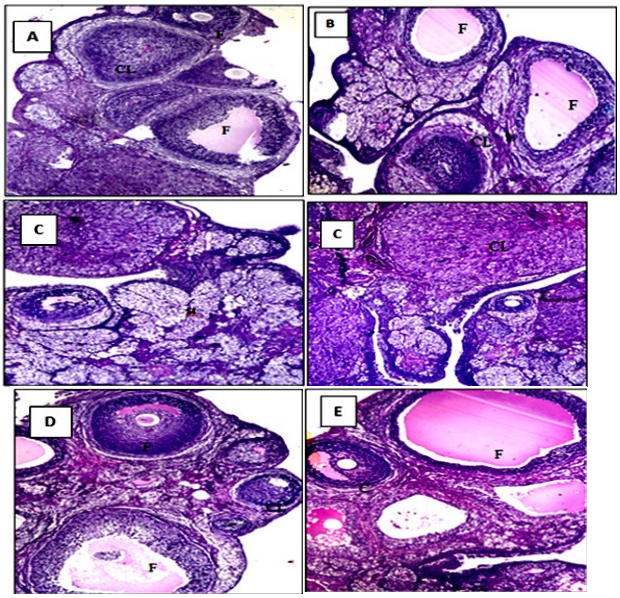

Figure 1. Histological structure of ovaries in all groups of the experiment. **(A)** Young female group: **(B)** old female group: **(C)** irradiated group: **(D)** cherry group: and **(E)** cherry+ irradiation (Hematoxylin and Eosin [H&E], X16).

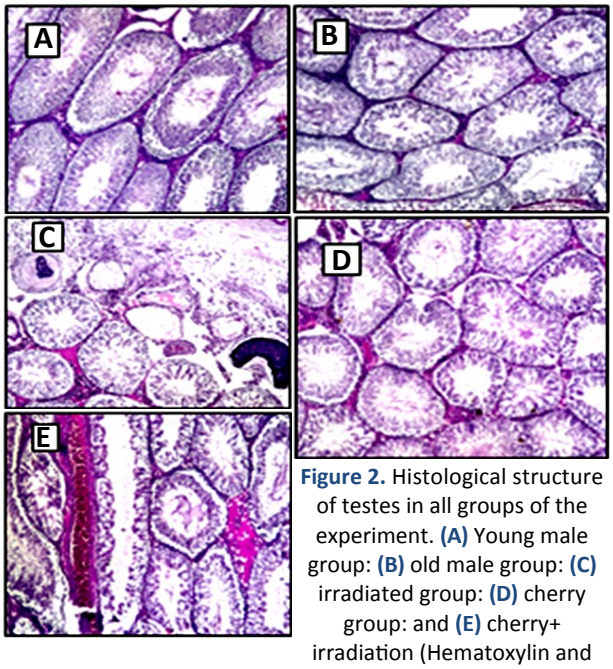

Figure 2. Histological structure of testes in all groups of the experiment. **(A)** Young male group: **(B)** old male group: **(C)** irradiated group: **(D)** cherry group: and **(E)** cherry+ irradiation (Hematoxylin and Eosin [H&E], X16).

DISCUSSION

Aging can be defined as an increase in mortality and/or decrease in fertility with age. In the existing study, we study the anti-aging effects of cherry juice on the reproductive ability of 20- month- old male and female irradiated rats through the evaluation of reproductive hormones. E2, the most active compound in estrogen, is secreted mainly from follicles in the ovary. By aging, inadequate ovarian follicle tissue failed to secrete the periodic E2. Estrogen has an important role in reproduction and controls ovary function, oocyte maturity, and the development of the endometrial membrane [34]. Hormones such as T [35], growth hormone, and IGF-1, usually decrease with age in both men and women [7]. In line with these previous studies, our data showed a decline in ovarian function of old rats. These results correlate with reproductive evaluation, as the data showed a decrease in the percentage of pregnancies of OAF compared to YAF. Numerous studies have shown that members of the IGF family are promoters of ovarian steroidogenesis [36-37]. IGF signaling also increases luteinizing hormone (LH) receptor mRNA transcription and boosts LH-induced upregulation of STAR mRNA transcription and consequently E2 production [38].

Rats treated with cherry juice alone had a significantly higher number of pregnancies. Cherry juice administration showed a significant amelioration of aged female (irradiated or non-irradiated rats) biochemical markers. Collectively, we can conclude that, cherry juice controls the reproductive ability of female rats by increasing the production of IGF-1, which, in turn increases estrogen synthesis and therefore improves ovarian function. Conversely, fractionated doses of γ-irradiation failed to improve ovarian function. This biochemical finding was confirmed by histological observation, as the irradiated group showed multiple numbers of the CL, and massive interstitial stromal cells with fewer follicles were detected in both the cortex and medulla of the ovary. Irradiated rats treated with cherry recorded non- histological change, observing different stages of the follicles with CT indicating that cherries possess a radioprotective effect.

This study further indicated an alteration in old male tested parameters. This is similar to previous studies, where investigators noted a decline in the blood T level and STAR protein in Leydig cells of aged males [35], [39, 40]. Rats treated with cherry juice showed a significant amelioration in the expression of the STAR gene and the levels of T and FSH in testis of aged rats whether irradiated or none. Testosterone is mainly manufactured in testicular Leydig cells from cholesterol and released into the blood circulation [41]. STAR protein controls the flow of cholesterol to the mitochondrial inner membrane for testosterone biosynthesis, and therefore STAR is a rate- limiting-step [42]. Patients exposed to diagnostic radiation should postpone for at least two spermatogenesis cycles before mating even, the diagnostic dose is too low to induce assessable hazard [43].

The obtained results of MDA and GSH in both uterus and testes were in agreement with Ferrucci and Studenski [7], who reported an increase in oxidative stress with aging owing to an intensification in production of ROS, possibly because of a decrease in the concentration and effectiveness of antioxidant buffers. Oxidative stress is a significant age-related risk factor that can injure ovarian utility by decreasing mitochondria activity [42], thus initiating cytoplasm deterioration and fall in

[DOI: 10.52547/ijrr.20.4.11]

antioxidant potential. In the ovary, these variations damage the fertilization and development of oocytes [43].

Additionally, old male rats exposed to γ-irradiation alone displayed a significant decrease in testes GSH as compared to young adult male rats. This result was supported by Shaban *et al.* [44], who reported a decrease in GSH next exposure to gamma radiation. The lessening in GSH is probably owing to the augmentation in ROS [45].

Combination treatment of OAM with cherry juice and doses of irradiation showed a significant reduction in testis and uterus MDA levels. Haidari *et al.* [26] reported that oral administration of tart cherry juice led to a significant reduction in MDA concentration. MT has cytoprotective effects that promote cell survival, with defenses against oxidative stress [46]. MT responds to various sorts of stress, comprising heavy metal toxicity, drug side effects, viral poison, endoplasmic reticulum (ER) stress, and oxidative stress [47-51]. Results of this study were supported by Mocchegiani *et al.* [52], who reported that MT is vital for immune efficiency during aging and age-related diseases. The increase in MT might help healthy aging outcomes because of its regenerative effects [53]. Cherries are fruits that contain a phenolic compound identified as anthocyanin that works as a potent antioxidant and anti-inflammatory for humans [18]. Endogenous ROS have been essential roles as signaling molecules through ovulation. ROS are vital signs in the beginning of apoptosis in antral follicles and granulosa cells of antral follicles by diverse stimuli, exposure to exogenous toxicants and ionizing radiation. Antral follicles, fertilization, and embryonic change may be mainly sensitive to exposure to ecological stimulants and chemical toxicants that boost oxidative stress [54]. From the viewpoint of anti- aging, one main objective is to prevent a decrease in ovum and ovarian follicles and therefore to compensate for a decline in estrogen secretion with a particular treatment [55].

CONCLUSION

The present study indicates that aging has a negative effect on reproductive hormones through inducing oxidative stress. Cherry juice ameliorates this negative effect of aging by reducing oxidative stress parameters, and hence improving female E2, FSH, and IGF-1 and male T, FSH, and STAR. The more pronounced effects were been observed in OAM (it should be noted that cherry demonstrated anti-aging effect in OAM more than in OAF). The obtained data shows that tart cherry juice can improve reproductive ability, especially for those undergoing radiotherapy.

ACKNOWLEDGMENTS

The authors are kindly indebted to the work members of gamma irradiation unit (NCRRT) for their generous support in carrying out the experimental irradiation. Appreciation and thanks are extended to Dr. Adel Bakeer Kholoussy, Professor of Pathology, Cairo University, Egypt, for his efforts in the histopathological examination.

***Conflicts of interest*:** There are no conflicts of interest to declare.

***Ethical Consideration*:** All animal techniques were achieved agreeing to the Ethics Committee of the National Research Center for Radiation Research and Technology (NCRRT), (No: 7A/18), Atomic Energy Authority.

***Funding*:** Authors received no financial support for the research, authorship, and/or publication of this article.

***Authors' Contribution*:** All authors were participated in the preparation of the paper equally.

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[DOI: 10.52547/ijrr.20.4.11]

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[DOI: 10.52547/ijrr.20.4.11]

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[DOI: 10.52547/ijrr.20.4.11]